RELATIVE RATES OF ABSTRACTION OF CHLORINE BY PHENYL RADICALS FROM N-CHLORAMIDES

by

SISTER MARY THERESE BLECHA

B. S., Marymount College, 1965
M. S. T., University of North Dakota, 1971

A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1976

Approved by:

Major Professor

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

I. Introduction and Literature Survey

It was the purpose of this study to determine the relative rates of chlorine abstraction from various N-chloro-N-substituted amides and to probe the facility with which amido radicals might undergo decomposition via a unimolecular β-elimination reaction. The formation and subsequent reactions of acylamino or amido radicals have been the subject of several studies including photolytic investigations on the N-nitrosamides, RCON(NO)R',[1-4] and the N-halamides, RCONXR'.[5-9] In most of these studies the R and R' groups were simple alkyl or aryl groups and the major subsequent reaction of the amido radical was one of hydrogen abstraction with formation of the parent amide. There was also some α-hydrogen elimination resulting in an alkylidenimide[2] which was isolated in the trimer form (eq. 1). In the studies where

(1) $$CH_3(CH_2)_4-\overset{O}{\overset{\|}{C}}-\underset{NO}{N}-CH_3 \xrightarrow{h\nu} CH_3(CH_2)_4-\overset{O}{\overset{\|}{C}}-\dot{N}-CH_3 \longrightarrow \left[CH_3(CH_2)_4-\overset{O}{\overset{\|}{C}}-N=CH_2\right]_3$$

R and/or R' were alkyl chains of four or more carbons, photolytic rearrangements occurred yielding isomeric 4-nitrosamides[2] with the nitroso group on the alkyl portion of the amide (eq. 2). Similar

(2) $$CH_3-\overset{O}{\overset{\|}{C}}-\underset{NO}{N}-(CH_2)_3CH_2CH_2CH_3 \xrightarrow[C_6H_6]{h\nu} CH_3-\overset{O}{\overset{\|}{C}}-\dot{N}-(CH_2)_3CH_2CH_2CH_3 \longrightarrow$$

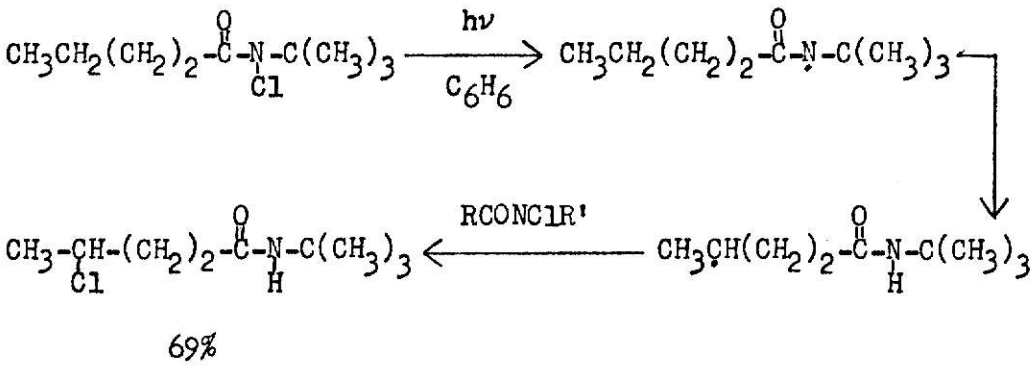
$$\left[CH_3-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-(CH_2)_3-\underset{NO}{CH}-CH_2CH_3\right]_2 \xleftarrow{NO} CH_3-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-(CH_2)_3\dot{C}HCH_2CH_3$$

37%

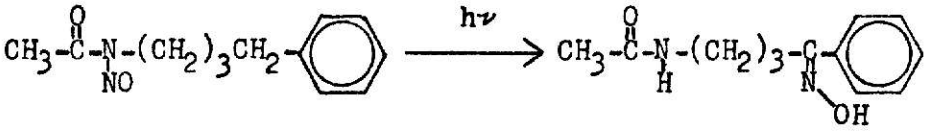
THIS BOOK CONTAINS NUMEROUS PAGES WITH DIAGRAMS THAT ARE CROOKED COMPARED TO THE REST OF THE INFORMATION ON THE PAGE.

THIS IS AS RECEIVED FROM CUSTOMER.

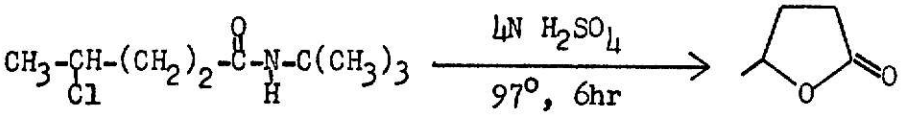
rearrangements occurred in the N-halamides[9] with the halogen ultimately residing on the C-4 in the acyl portion of the amide (eq. 3). In other

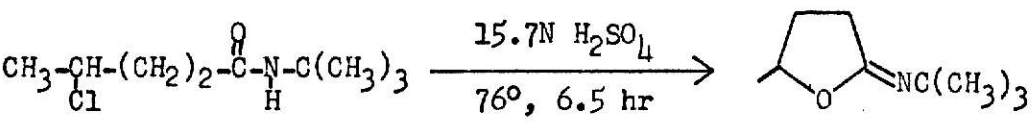
(3) 

instances an oximino amide[2] was formed and where cyclization was more favored lactone,[9] iminolactone,[9] or oxazoline[9] resulted. The oximino amide resulted (eq. 4) from photolysis of a nitrosamide in petroleum

(4) 

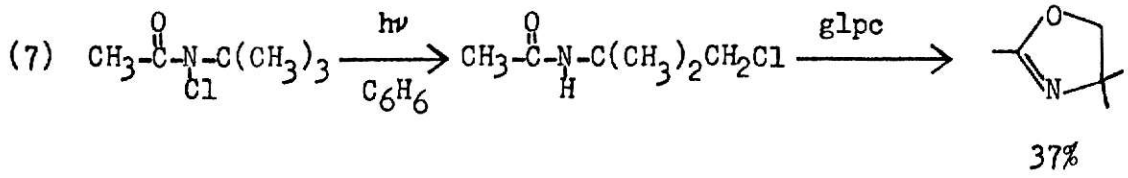
ether by a mechanism similar to that shown in equation 2. The lactone and iminolactone were formed (eqs. 5 & 6) by acid treatment

(5) 

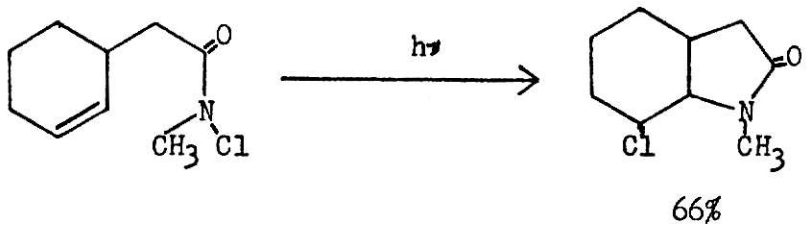
(6) 

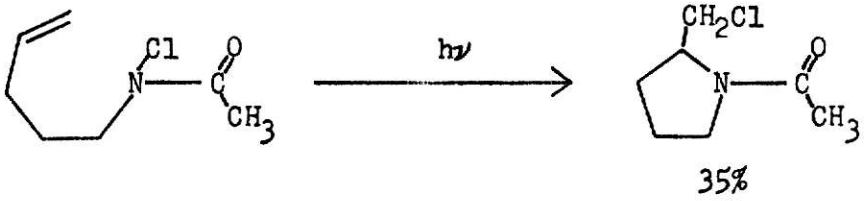
of the rearranged product in eq. 3. The oxazoline was formed (eq.7) during the glpc analysis of reaction products from the photolysis of

N-chloro-N-tert-butylacetamide. Kuehne and Horne[7] have shown that

(7) 

photolytic cyclization of olefinic N-chloramides results in the formation of chlorine substituted lactams and N-heterocyclic amides (eqs. 8 & 9).

(8) 

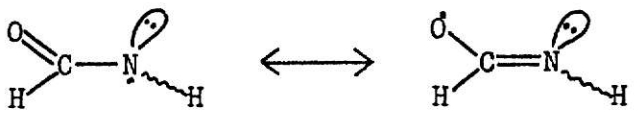
(9) 

Since these stereospecific intramolecular hydrogen abstraction reactions have been shown to give fairly good yields, more emphasis has been placed on the study of their usefulness in organic syntheses rather than on the investigation of the amido radicals involved. The amido radical, its formation, structure, and reactivity, is of considerable importance not only in the above synthetic reactions but also because of the consequences of its possible formation in biological systems.

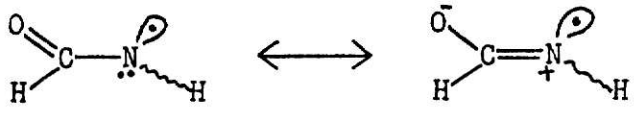
The amide bond is a very common and essential chemical bond in living systems since it is responsible for linking the amino acids into protein molecules. The amide functional group could potential-

ly be transformed into an amido radical by a free radical attack from the normal pool of free radicals present in the living system, or by some type of high frequency radiation such as ultraviolet, x-rays, or gamma rays. The subsequent reaction of this amido radical could cause denaturation of the protein and thus could lead to serious consequences depending on the type of protein involved.

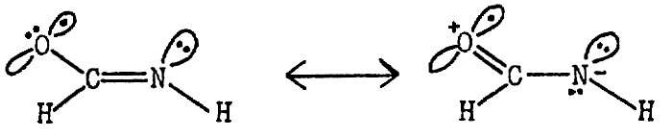
Whereas the electronic features of free radicals formed from most common organic functional groups have been rather well-characterized, there has been much controversy as to the electronic structure of the ground state of the amido radical. On the basis of semiempirical INDO calculations, Koenig, et al.,[10] presented three possible structures for the amido radical. In the π radical (10) the unpaired electron is



(10)



(11)

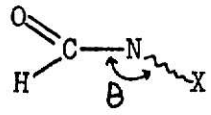


(12)

capable of entering into conjugation with the π bond of the carbonyl group while in the $\sum_N$ radical (11) it is the lone pair that enters into the conjugation with the carbonyl bond. The $\sum_O$ radical (12) results from the unpaired electron residing on the oxygen atom with the

oxygen donating a lone pair of electrons to the OCN conjugated system.

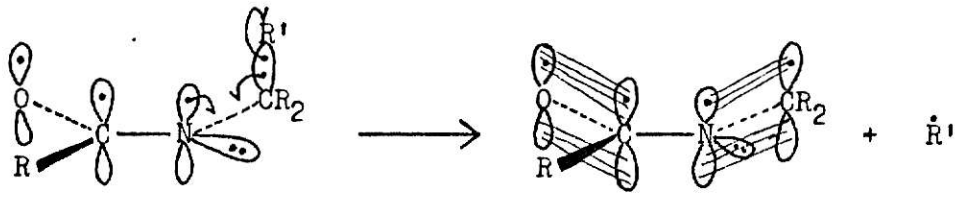
Koenig, et al.,[10] were concerned with the C-N-X angle, θ, and the dependence of the structure of the amido radical on θ. The INDO cal-

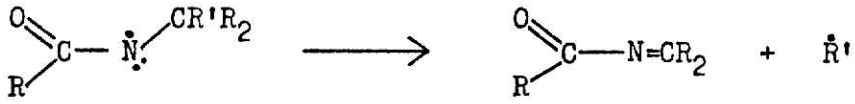


culations performed for the formamido, N-hydroxy formamido and N-methyl formamido radicals showed the π radical to be the more favored structure with $\theta \sim 114\text{-}120^{\circ}$. In the case where $X=CH_3$ the π radical was still favored but by a lower energy value. From this they predicted the possibility of steric effects causing the angle to increase and tending toward the more favorable Σ_N at $\theta = 180^{\circ}$.

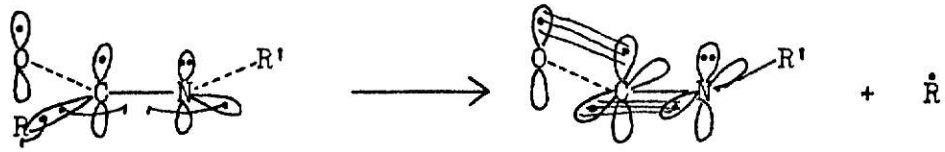
In 1972, Danen and Gellert[11] published evidence which suggested that the amido radical exists in the π electronic state. This was the result of an esr study of N-chloro-N-methyl-t-butylamide and N-chloro-N-t-butylacetamide. Although their results suggested a π electronic ground state it was also evident that there was little delocalization of the unpaired electron into the carbonyl π system. A related C^{13}-CIDNP study[12] in 1975 on the N-methylbenzamido radical supported the π electronic ground state. Danen and Neugebaur[13] have compiled a review on various amino free radicals including discussions of reactivities, reaction types, and structure.

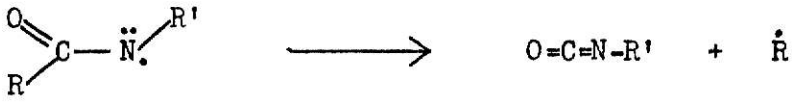
The electronic structure of the amido radical is important in determining its subsequent reactions, particularly β-scission reactions. If the π radical is favored β-scission would more likely occur in the N-alkyl group forming an alkylidenimide (eqs. 13 & 14).

(13) 

(14) 

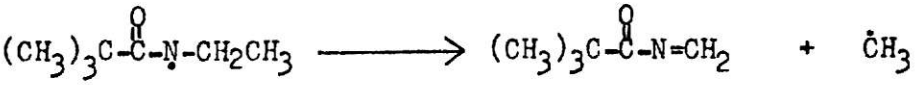
β-Scission of the acyl portion with formation of an isocyanate would be the more favored reaction of the Σ_N radical (eqs. 15 & 16). In

(15) 

(16) 

view of either type of β-scission occurring in a peptide linkage it could result in the less of a substituent group or the complete scission of the peptide chain.

Evidence of alkyl β-scission has previously been detected by both Gellert[14] and West[15] in this laboratory in their esr studies of amido radicals. Gellert obtained esr evidence of β-scission occurring in the N-ethylpivalamido radical by the presence of the methyl radical (eq. 17). West obtained evidence of a similar β-scission

(17) 

using ethyl-N-methoxycarbamate which formed carboethoxymethyl nitroxide presumably via methyl elimination and then recombination (eq. 18).

(18) $C_2H_5O-\overset{O}{\overset{\|}{C}}-\dot{N}-O-CH_3 \longrightarrow C_2H_5O-\overset{O}{\overset{\|}{C}}-N=O + \dot{C}H_3 \longrightarrow C_2H_5O-\overset{O}{\overset{\|}{C}}-\overset{\cdot\cdot}{N}-CH_3$

As noted above it was the purpose of this study to determine the relative rates of chlorine abstraction from N-chloro-N-substituted amides and, secondly, to probe briefly into the facility by which amido radicals undergo decomposition via β-elimination. The chlorine was abstracted by phenyl radicals formed from the decomposition of phenylazotriphenylmethane (PAT) at 60°C. An extensive search of the literature did not reveal any type of study dealing with the relative rates of formation of substituted amido radicals.

The halogen abstraction method of forming a radical is an extremely valuable method to use when a specific radical site is desired.[16] Although hydrogen abstraction by free radicals has been studied extensively, most compounds have two or more abstractable hydrogens and hence, the site of radical formation may be indefinite if formed by hydrogen abstraction. Using the hydrogen abstraction method on the N-monosubstituted amides, the more facile abstraction would be that of the hydrogen from the α-carbon of the N-alkyl group or the acyl group rather than from the nitrogen. Such results were obtained by Hayon, et al.,[17] in their studies of hydrogen abstraction from amides using the hydroxyl radical in an aqueous system. Their results showed that in certain amides the rate of hydrogen abstraction from either α-carbon (19 or 20) was an order of magnitude greater than from the

$R-\dot{C}H-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-CH_3$ (19)

$R-CH_2-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-\dot{C}H_2$ (20)

$R-CH_2-\overset{O}{\overset{\|}{C}}-N-CH_3$ (21)

nitrogen (21). Therefore the need existed to use the halogen abstraction method on the N-chloro-N-substituted amides to be certain that the amido radical was being formed. Since N-chloramides are not difficult to prepare, this is a convenient method of generating the amido radical by an abstraction technique.

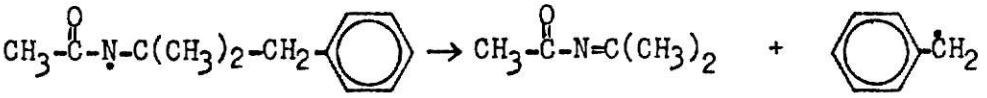
As mentioned previously a search of the literature revealed that most amido radical reaction studies have been concerned with hydrogen abstraction either intramolecularly or intermolecularly from the amide or the solvent. In this study the solvent used primarily was benzene which is a poor hydrogen atom donor[3] and the N-chloramides chosen for study were such that intramolecular hydrogen abstraction was unlikely. Therefore major consideration was given to β-scission and to intermolecular hydrogen abstraction from the amide.

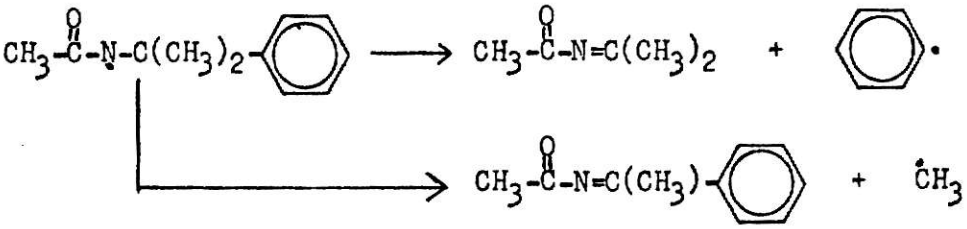
It has been shown in studies of peroxide decomposition[18] that where β-scission is more highly favored the rate is greatly increased. This is shown by the following reaction rate comparisons (eqs. 22-24).

	Peroxide	Relative Rate
(22)	$\underline{t}\text{-BuO-O-}\overset{\overset{O}{\|}}{C}\text{-CH}_3 \longrightarrow \underline{t}\text{-BuO}\cdot + \cdot\text{O-}\overset{\overset{O}{\|}}{C}\text{-CH}_3$	1
(23)	$\underline{t}\text{-BuO-O-}\overset{\overset{O}{\|}}{C}\text{-CH}_2\text{Ph} \longrightarrow \underline{t}\text{-BuO}\cdot + CO_2 + \cdot\text{CH}_2\text{Ph}$	1,340
(24)	$\underline{t}\text{-BuO-O-}\overset{\overset{O}{\|}}{C}\text{-CH(Ph)}_2 \longrightarrow \underline{t}\text{-BuO}\cdot + CO_2 + \cdot\text{CH(Ph)}_2$	22,000

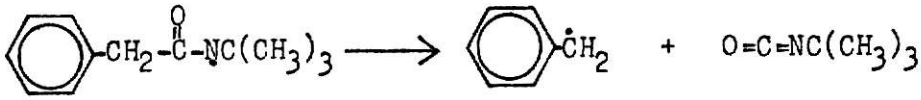
Since β-scission is possible in the N-chloramides then it is logical to assume that where the R and R' groups would easily lend themselves to a concerted β-scission the rate of chlorine abstraction should

increase. For example in N-chloro-N-(1,1-dimethyl-2-phenethyl)acetamide where β-scission would result in a relatively stable benzyl radical (eq. 25) this rate would be faster than in N-chloro-N-α,α-dimethylbenzylacetamide where β-scission would result in a destabilized phenyl radical or methyl radical (eq. 26). In the other

(25) 

(26) 

type of β-scission, that more similar to the perester decomposition, the rate would be faster for the N-chloro-N-t-butylphenylacetamide resulting in a stabilized radical (eq. 27) than for N-chloro-N-t-butylbenzamide resulting in a destabilized radical (eq. 28). The

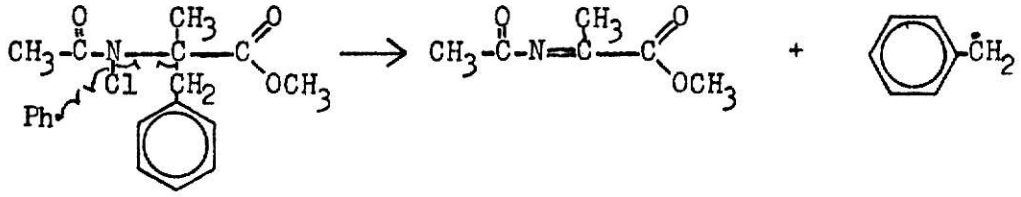
(27) 

(28) 

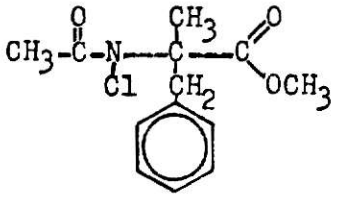
stabilized radical[19] has a positive stabilization energy and allows for delocalization of the unpaired electron while the destabilized radical has a negative stabilization energy and does not allow for delocalization of the unpaired electron. The stabilization energies of these two types of radicals are defined in reference to that for the ethyl radical which is zero. Since the stabilization energy of the stabilized radical is positive, β-scission resulting in a sta-

bilized radical would be more likely to occur than where it would result in a destabilized radical.

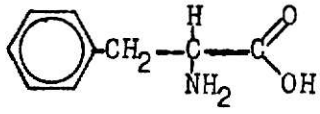
By combining the driving forces of a concerted β-scission and of the formation of a conjugated -enedione system the rate of chlorine abstraction could conceivably be greatly increased. The rate of chlorine abstraction from N-chloro-N-(1-methyl-1-benzyl methylacetate) acetamide (eq. 29) could be much greater than in the case of where

(29) 

only a benzyl radical is eliminated. This particular N-chloramide (30) has a structure similar to a dipeptide. It contains in part the common



(30)



(31)

amino acid phenylalanine (31). Although it would be necessary to methylate the α-carbon and esterify the carboxyl group of this amino acid in the N-chloramide to prevent undesirable side reactions in the present studies, the benzyl moiety would still be free for β-elimination. Rates of chlorine abstraction from these types of N-chloramides could give some indication as to types and rates of amido radical reactions possible in proteins.

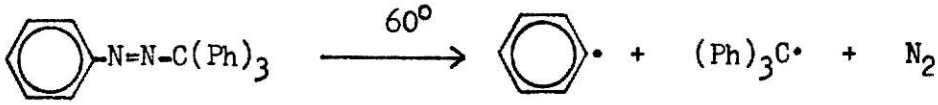
II. Kinetic Studies

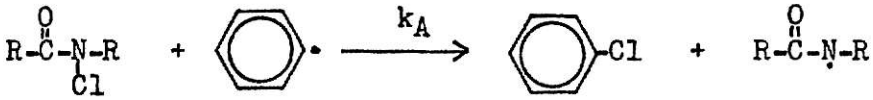
A. Results

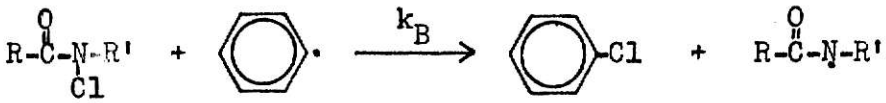
The N-chloro-N-substituted amides were prepared by a reaction of the parent amide with tert-butylhypochlorite in carbon tetrachloride solvent[9] (eq. 32). Several amides proved difficult to chlorinate in which case tert-butylhypochlorite was used also as the solvent with a few drops of bromine added as a catalyst.

(32) $$R\text{-}\overset{O}{\overset{\|}{C}}\text{-}\underset{H}{N}\text{-}R' \xrightarrow[\text{or } t\text{-BuOCl, } Br_2 \text{ (trace)}]{t\text{-BuOCl, } CCl_4} R\text{-}\overset{O}{\overset{\|}{C}}\text{-}\underset{Cl}{N}\text{-}R'$$

Phenyl radicals were generated by the thermal decomposition of phenylazotriphenylmethane (PAT) at 60°C in benzene solvent (eq.33) with the presence of two N-chloramides, A (eq. 34) and B (eq. 35).

(33) 

(34) 

(35) 

With both N-chloramides available for attack by the phenyl radical a measure of the initial and final concentrations of both N-chloramides would indicate the relative rate of chlorine abstraction. It was not necessary to determine the exact initial and final concentrations since the ratio of initial to final concentration could be used to calculate

the relative rate constants. This ratio was determined by integration of appropriate peaks in the nmr spectra. An internal standard was used in the recording of each nmr spectrum to eliminate error introduced by the nmr spectrometer. The ratios of the area of one peak of amide A to the internal standard S before (A_o) and after (A_t) the reaction were calculated. The log of the two ratios calculated for amide A was divided by the log of the two ratios calculated for amide B (eq. 36) to determine k_A/k_B, the relative rate ratio.

$$\frac{\log \dfrac{(A_o/S)}{(A_t/S)}}{\log \dfrac{(B_o/S)}{(B_t/S)}} = k_A/k_B \tag{36}$$

This equation was proposed by Bunnett[20] for use where there is direct competition between two reactants for the attack of a third reactant. If it is first order in F and first order in both A and B then it is a second order reaction and equation (37) may be used if the

$$F + A \longrightarrow X$$

$$F + B \longrightarrow X$$

$$\frac{-d[A]}{-d[B]} = \frac{k_A[A]}{k_B[B]} \xrightarrow{\text{integration}} (37) \quad \frac{\log [A]_o/[A]_t}{\log [B]_o/[B]_t} = k_A/k_B$$

concentrations of both A and B change appreciably in the reaction. This same equation was successfully used by Walsh and Kuivila[21] in determining competitive rates of halogen abstraction from aryl and alkyl halides using the tri-n-butyl tin radical.

Though the use of this nmr technique in determining the ratios of initial and final concentrations was a relatively easy method to use there were certain disadvantages involved, namely peak overlap and inability to get good resolution on some of the spectra. For some N-chloramides the relative rates could not be calculated due to nearly identical chemical shifts occurring in the two N-chloramides thus causing a complete peak overlap.

There were at least four runs and usually six runs performed in determining each rate ratio value. The standard deviation was calculated according to equation (38)[22] for each set of runs and varied from 0.045 to 0.46 with the average value being ca. 0.19. To

$$S = \sqrt{\frac{\sum(X_n - \bar{X})^2}{(n - 1)}} \qquad (38)$$

n = number of runs
X_n = rate ratio for run number n
$\bar{X}$ = average rate ratio

determine whether a rate ratio value for a certain run, X_n, should be retained equation (39)[22] was used. If the t_i was greater than the

$$t_i = \frac{|X_n - \bar{X}|}{R} \qquad (39)$$

X_n = rate ratio value in question
$\bar{X}$ = average rate ratio
R = range of rate ratio values

theoretical value of t_i for a given n value then the X_n value must be discarded. Applying this method to the obtained data it was found that none of the X_n values had to be eliminated. Therefore, it seems that the method used in obtaining the rate ratios was reliable although the results exhibited somewhat less precision than ideally desired.

The first series of N-chloramides studied was that of the rate of chlorine abstraction from N-chloro-N-tert-butylacetamide compared to that of N-chloro-N-methylacetamide, N-chloro-N-1,1-dimethyl-2-phenethylacetamide and N-chloro-N-α,α-dimethylbenzylacetamide (Table I).

Table I

Relative Rate of Chlorine Abstraction from Representative N-Chloramides

Amide: RCONClR'		Relative Rate
R	R'	
CH_3	$C(CH_3)_3$	1.00
CH_3	CH_3	0.641
CH_3	$C(CH_3)_2CH_2Ph$	1.22
CH_3	$C(CH_3)_2Ph$	1.28

The results showed that even though β-scission is favorable where R' = $C(CH_3)_2CH_2Ph$ the relative rate of chlorine abstraction was similar to the amide R' = $C(CH_3)_2Ph$ for which a concerted elimination was unlikely. These preliminary data suggested a steric influence on the rates of chlorine abstraction.

Since the preliminary data did seem to follow the trend of increased rate with increased bulkiness of R', such a series of N-chloro-N-substituted amides was synthesized and subjected to chlorine abstraction. The results are tabulated in Table II. Rates relative to both N-chloro-N-methylacetamide and to N-chloro-N-tert-butylacetamide were calculated. Throughout the remainder of this paper reference will be made only to the rates relative to N-chloro-N-methylacetamide. This amide was preferred because of considerable overlap of

Table II

Relative Rates of Chlorine Abstraction by the Phenyl Radical from N-Chloramides at 60°C

No. n	R	Amide: RCONClR' R'	k_1/k_n [a]	S [b]	R [c]	k_7/k_n [d]	S [e]	C [f]
1.	CH_3	CH_3			1.00	1.56	0.33	
2.	CH_3	CH_2CH_3	2.48	0.46	0.40			
3.	CH_3	$CH_2CH_2CH_3$	1.59	0.17	0.63			
4.	CH_3	CH_2CH_2Ph	1.17	0.19	0.86	1.62	0.21	0.722
5.	CH_3	$CH(CH_3)_2$	1.15	0.18	0.87			
6.	CH_3	$CH_2C(CH_3)_3$	0.944	0.23	1.05	1.36	0.18	0.694
7.	CH_3	$C(CH_3)_3$	0.641	0.33	1.56			
8.	CH_3	$C(CH_3)_2CH_2Ph$	0.524[g]		1.91	0.817	0.04	
9.	CH_3	$C(CH_3)_2Ph$	0.498[g]		2.01	0.777	0.11	
10.	CH_3	$C(CH_3)(COOCH_3)CH_2Ph$	0.341	0.045	2.93			
11.	$PhCH_2$	$C(CH_3)_3$	0.462	0.15	2.16	0.752	0.27	0.614
12.	Ph	$C(CH_3)_3$	0.265	0.057	3.77			
		Amine						
13.	N-chloro-2,2,6,6-tetramethylpiperidine		1.31	0.23	0.76			

Table II continued,

a The experimentally determined rate ratio of N-chloro-N-methylacetamide to the n N-chloramide.

b The calculated standard deviation of the experimentally determined rate ratio in a.

c The rates of chlorine abstraction relative to N-chloro-N-methylacetamide.

d The experimentally determined rate ratio of N-chloro-N-tert-butylacetamide to the n N-chloramide.

e The calculated standard deviation of the experimentally determined rate ratio in d.

f The cross-check value calculated from equation 40.

g These two rate ratios are calculated values from the experimentally determined k_7/k_8 and k_7/k_9 values by the use of the cross-check value. They were not determined directly due to lack of sufficient amount of the N-chloramides 8 and 9.

peaks of different amides with N-chloro-N-tert-butylacetamide on the nmr spectra. However this latter amide was used where possible to serve as a cross-check on the relative rates. The cross-check value was calculated according to equation (40). There was a need for this

$$\frac{k_1/k_n}{k_7/k_n} = k_1/k_7 \qquad (40)$$

control to eliminate the possibility of any secondary reaction affecting the relative rate value. If the calculated cross-check value was similar to the experimental value, 0.641, then it could be assumed that there were no secondary reactions affecting the rate of abstraction.

It is possible in these reactions that HCl could be formed. This could cause a significant change in the rate of chlorine abstraction

by its ability to convert the N-chloramide to the parent amide (eqs. 41-44). In order to check the presence of HCl and any effect it might

(41) $$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}\underset{\underset{Cl}{|}}{N}\text{-}CH_3 \longrightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}N{=}CH_2 + HCl$$

(42) $$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}\underset{\underset{Cl}{|}}{N}\text{-}R' + HCl \longrightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}\underset{\underset{H}{|}}{N}\text{-}R' + Cl_2$$

(43) $$R\cdot + Cl_2 \longrightarrow RCl + Cl\cdot$$

(44) $$Cl\cdot + RH \longrightarrow R\cdot + HCl$$

have on the reaction rate sodium carbonate was added in excess to three of the reaction ampoules. The rate ratio values obtained for k_1/k_7 were 0.595, 0.694 and 0.567 and were well within the range of the k_1/k_7 values previously obtained.

To check the fact that the relative rate was not dependent on the concentration of the N-chloramides A and B the ratio of $[A]_o/[B]_o$ was varied from ca.0.5 to 2.0. The relative rate values obtained were independent within experimental error of the concentration ratio.

To determine whether there was a rate dependence on both steric and inductive effects a multiple regression analysis was run on part of the experimental data as illustrated in Table III. Correlations obtained by varying the input data are shown in Table IV.

Infrared spectra were recorded on the Perkin-Elmer Model 180 Spectrophotometer for an accurate determination of the C=O stretching frequency in a few representative N-chloramides for the purpose of estimating relative amounts of C-N double bond character. The results of these spectra are listed in Table V.

Table III

Data Used in Multiple Regression Analysis

Amide: RCONClR' R	R'	k_1/k_7	E_s [a]	σ^* [a]
CH_3	CH_3	1.00	0.00	0.000
CH_3	CH_2CH_3	2.48	-0.07	-0.100
CH_3	$CH_2CH_2CH_3$	1.59	-0.36	-0.115
CH_3	CH_2CH_2Ph	1.17	-0.38	+0.080
CH_3	$CH_2C(CH_3)_3$	0.944	-1.74	-0.165
CH_3	$CH(CH_3)_2$	1.15	-0.47	-0.190
CH_3	$C(CH_3)_3$	0.641	-1.54	-0.300

a These values were taken from reference (24).

Table IV

Correlations Obtained from the Multiple Regression Analysis by Varying Input Data

1. Including N-chloro-N-methylacetamide:

   (a) E_s and σ^*

   $$\log k_1/k_n = -0.18\,\sigma^* + 0.20\,E_s + 0.18 \qquad r = 0.672$$

   (b) σ^* only

   $$\log k_1/k_n = 0.54\,\sigma^* + 0.13 \qquad r = 0.360$$

   (c) E_s only

   $$\log k_1/k_n = 0.18\,E_s + 0.19 \qquad r = 0.665$$

2. Excluding N-chloro-N-methylacetamide:

   (a) E_s and σ^*

   $$\log k_1/k_n = -0.0013\,\sigma^* + 0.23\,E_s + 0.26 \qquad r = 0.820$$

Table IV continued,

(b) σ^* only

$$\log k_1/k_n = 0.76\sigma^* + 0.18 \qquad r = 0.478$$

(c) E_s only

$$\log k_1/k_n = 0.23\ E_s + 0.26 \qquad r = 0.820$$

Table V

The C=O Stretching Frequency of N-Chloramides

Amide: R	RCONClR' R'	Frequency (cm^{-1})
CH_3	CH_3	1680
CH_3	$C(CH_3)_3$	1680
$PhCH_2$	$C(CH_3)_3$	1672
Ph	$C(CH_3)_3$	1675

After completion of the relative rate determinations and a brief study of reaction products the question arose as to whether an equilibrium was being established during the chlorine abstraction reaction between an N-chloramide and the parent amide of the other competing N-chloramide (eq. 45). To determine whether this reaction was occurring

(45) $$R-\overset{O}{\overset{\|}{C}}-\underset{Cl}{N}-R + R-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-R' \underset{\leftarrow}{\overset{K_{eq}}{\rightarrow}} R-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-R + R-\overset{O}{\overset{\|}{C}}-\underset{Cl}{N}-R'$$

representative N-chloramides and parent amides were reacted as indicated in Table VI. The reaction ampoules were prepared in the same

Table VI

Equilibrium Constant Values for the Chlorination of an N-Alkylacetamide by an N-Chloro-N-alkylacetamide

Ampoule	Amide	K_{eq}
1	N-methylacetamide N-chloro-N-ethylacetamide	1
2	N-ethylacetamide N-chloro-N-methylacetamide	1
3	N-phenethylacetamide N-chloro-N-methylacetamide	1
4	N-methylacetamide N-chloro-N-t-butylacetamide	10.6[a]
5	N-t-butylacetamide N-chloro-N-methylacetamide	.006[a]

a These should be reciprocal values. Perhaps the equilibrium was not yet established.

manner and subjected to the same conditions as those used in the relative rate studies with the exception of no PAT being present. The K_{eq} values (eq. 45) for the reactions listed in Table VI were obtained from measurements of the peak heights on the nmr spectra.

The results in Table VI show that an equilibrium reaction (eq. 45) does occur. To determine whether this equilibrium had a significant affect on the relative rate ratios obtained in the competitive rate studies using the phenyl radical, hypothetical k_A/k_B ratios were calculated for different initial concentration ratios, $[A]_o/[B]_o$, assuming $K_{eq} = 10$. If the calculated k_A/k_B ratios varied according to the $[A]_o/[B]_o$ ratios, then it could be concluded that the equilibrium (eq. 45) did not significantly affect the observed relative rate of chlorine abstraction by the phenyl radical since it had been shown previously that this value was insensitive to the ratio

of the competing N-chloramides.

These calculations were performed by assuming that all phenyl radicals abstracted chlorine with the parent amide being formed by hydrogen abstraction. This gave the two competitive reactions (eq. 46 & 47). By allowing $[AH] + [BH] = 1$, and using allowed $[A]_o$ and $[B]_o$ values the $[A]_t$ and $[B]_t$ values could be calculated for these two reactions using the assumption that $k_A/k_B = 1.00$ in absence of any equilibrium. By combining the products of equations (46) and (47) the equilibrium reaction (eq. 48) could be written. The re-

(46) $$A_o \xrightarrow{k_A} A_t + AH$$

(47) $$B_o \xrightarrow{k_B} B_t + BH$$

(48) $$A_t + BH \underset{}{\overset{K_{eq}}{\rightleftharpoons}} B_t + AH$$

spective concentrations for the reactants and products in equation (48) at $K_{eq} = 10$ could be calculated by using the K_{eq} expression (eq. 49). As anticipated, changing the $[A]_o/[B]_o$ ratio with $K_{eq} = 10$

(49) $$K_{eq} = \frac{[B]_t\,[AH]}{[A]_t\,[BH]}$$

did have a noticeable change on the relative rate constant as shown in Table VII.

Control reactions were also run to check the possibility of other reactions occurring between the products and the two competing N-chloramides. The results showed no significant reaction.

Table VII

Relative Rate Ratios Resulting from Changes in the Initial Concentration Ratio Assuming $K_{eq} = 10$

$[A]_o/[B]_o$	k_A/k_B
0.5	6.09
1.0	5.14
2.0	8.14
10.0	10.5

B. Discussion

One of the most common ways of generating a free radical is by the abstraction of a univalent atom, either hydrogen or a halogen. This particular study is concerned with the abstraction of a halogen to specifically generate an amido radical.

The ease[16] with which halogen is abstracted from organic molecules is dependent on several factors. One of these is the bond strength and it is well known that the order of the rate of abstraction of the different halogens is as follows: $I > Br > Cl \gg F$ illustrating the fact that iodine has the weakest bond and fluorine has the strongest bond. This indirect relationship of rate of abstraction to bond strength is again illustrated in the following sequence of alkyl and aryl compounds, $3^{\circ} > 2^{\circ} > 1^{\circ} \sim Ar$, showing that the tertiary carbon-halogen bond is weaker than a primary or aryl carbon-halogen bond. The fact that the ratio of halogen to hydrogen abstraction from alkyl compounds was not as great as anticipated from bond energy considerations alone suggested that an increase in electron density on the carbon to

which the halogen was bonded tended to make free radical attack on the halogen more difficult. This fact was borne out in a study of polar effects. It was found that electron-donating substituents decrease the rate of halogen abstraction and increase the rate of hydrogen abstraction while electron-withdrawing substituents have the opposite effect. The above was concluded from use of the Hammett relationship in which a positive ρ value was obtained for halogen abstraction and a negative ρ value for hydrogen abstraction. The positive ρ value indicated that in the transition state the electron density on the carbon to which the halogen is bonded is increased relative to the ground state. Alternatively, an electron-withdrawing substituent on carbon may simply produce a weaker ground state carbon-halogen bond. Whether the substituent exerts its predominant effect on the ground state or the transition state the greater the capacity for the carbon to accept the electron density, the greater will be the rate of abstraction. Another factor shown to affect the rate of halogen abstraction is that of steric effects. An extensive review on halogen abstraction processes has been compiled by Danen.[16]

Although the above brief discussion of halogen abstraction dealt with homolytic cleavage of carbon-halogen bonds; much of it should be applicable to the homolytic cleavage of the nitrogen-chlorine bond. The bond energy of the N-Cl bond (NH_2-Cl = 60 $\pm$ 6 kcal/mol)[25] is less than that of the C-Cl bond (CH_3-Cl = 83.5 kcal/mol)[25] so from a consideration of bond energies one would conclude that the rate of chlorine abstraction from the nitrogen should be greater than from the carbon. But the fact that the nitrogen has a lone pair of electrons may affect

the rate of abstraction.

In comparing the rates of abstraction from amines and amides one would expect a faster rate from the amide because of possible resonance stabilization by the acyl group present as well as a favorable polar effect. The latter would tend to withdraw the lone pair from the nitrogen thus creating a partial positive charge on the nitrogen and increasing its capacity to accept an increase in electron density in the transition state for radical attack. This fact was shown to be true in the comparison of the rates of iodine abstraction from α-iodocarbonyl compounds vs. alkyl iodides.[26] The rate of iodine abstraction from the carbonyl compound was shown to be from 4 to 5 times faster than from the alkyl compound. Representative examples of the relative rate of iodine abstraction from aliphatic iodides to bromine abstraction from CCl_3Br (k_I/k_{Br}) are for CH_3CH_2I, $k_I/k_{Br} = 0.33$ and for CH_2ICOOH, $k_I/k_{Br} = 1.73$.

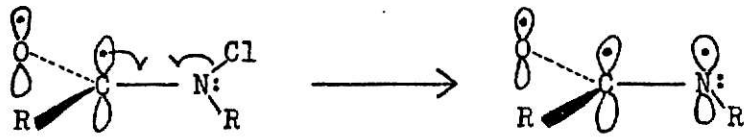
Steric effects can cause either a decrease in the rate by hindering the approach of the radical depending on its size or an increase by the release of steric strain during the formation of the radical. An example of the latter effect was observed in iodine abstraction from ortho-iodobenzenes.[27] The observed increase in the rate of iodine abstraction was as follows, 2-F < 2-Cl < 2-Br < 2-I, thus showing that the fastest rate occurred in the molecule with the greatest steric strain.

The general trend of relative rates in the series of amides listed in Table II shows there was no significant increase where a concerted β-scission could take place nor where a combination of concerted β-scission and formation of a conjugated -enedione sys-

tem is possible. Therefore, one must conclude from consideration of the relative rates that evidence of a concerted β-scission in these chlorine abstraction reactions was not present.

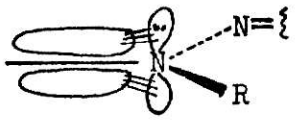
The general trend that was indicated in the amide series is that as R and/or R' get larger the rate increases. It was possible in this particular series of chlorine abstractions that the increase in size of the neighboring groups lowers the rotational barrier height of the C-N bond. This allows for the chlorine to be in a less hindered position for attack for a greater period of time, the least hindered position being at rotation of 90° out of the amide bond plane. The amide with the lower rotational barrier height would have a higher probability of being in such a conformation and, hence, should be more susceptible to abstraction.

The lower rotational barrier of the C-N bond would also favor formation of the π amido radical. In the π radical the unpaired electron is perpendicular to the $\rangle C\text{-}N\langle$ plane. As the $-N\langle_{Cl}$ group is rotated out of the plane and closer to 90° the N-Cl bond electrons move closer toward the carbonyl π bond plane thus allowing for the subsequent unpaired electron to enter directly into conjugation with the carbonyl π bond and form the π radical (eq. 50).

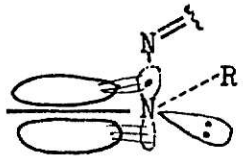
(50) 

Nelsen and Landis[28] showed that similar events occurred in their work with anilino radicals. They found that the rate of formation of these radicals was not as dependent on the electronic effects of substituents in the phenyl ring as it was on the conformational change.

They stated that the favored ground state conformation (51) where the one pair of electrons from the nitrogen is in conjugation with the aromatic π system would not be the favored transition state conformation (52) in which the unpaired electron is able to become delocal-



(51)

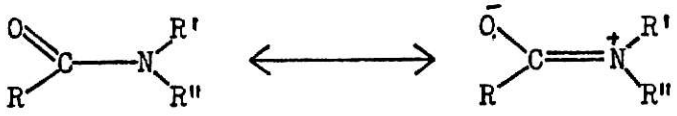


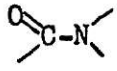
(52)

ized. Therefore a "twisting" out of the plane must occur. This twisting would be increasingly favored by larger R groups because of steric interactions with the phenyl ring. They were able to show that the decomposition rate for R = t-Bu ($k_{OCH_3}/k_H = 5.5$) was much less affected by substituents on the phenyl ring than for R = Me ($k_{OCH_3}/k_H = 24$).

It was, therefore, necessary to probe whether the rotational barrier height of the C-N bond in amides is a significant factor in the relative rates of chlorine abstraction. In amides the C-N bond possesses a certain amount of double bond character (eq. 53) as a result of a

(53)



favored planar structure for the  group in which sp^2 hybridization exists for th nitrogen bond with the nitrogen lone pair being in a 2p orbital. These 2p electrons are capable of conjugating with the π bond of the carbonyl group. The extent of conjugation or double bond character in the C-N bond depends on the electron-withdrawing or donating ability of the substituents R, R', R" and on the polarity of

the solvent or ions present in the solution. Since these factors affect the double bond character of the C-N bond then it is reasonable to assume that they also affect the barrier height to rotation about the C-N bond.

If R' and R" were different alkyl groups such as Me, Et, i-Pr, or t-Bu, there would be an increasing order of electron release and this should result in an increased bond order and an increase in the barrier height. If R' and/or R" were electron-withdrawing groups this should decrease electron density and thus decrease the bond order and the barrier height. This electronegativity effect was very evident in the work done by Cantacuzene, et al.[29] They found the rotational barrier in dimethylformamide to be 21.5 kcal/mol and that of N-fluoro-N-methylformamide to be 11.0 kcal/mol. The fluorine, due to its high electronegativity, reduced the electron density sufficently to diminish the barrier height by approximately one-half.

The polarity of a solvent may have a large effect on the barrier height because of the resonance form, $\bar{O}\!\!>\!\!C\!=\!\overset{+}{N}\!\!<$. The polar nature of a solvent could sufficiently stablize this form such that it would contribute relatively more to the resonance hybrid resulting in a higher rotational barrier. This was found to be true by Rao, et al.,[30] in their study of solvent effects on the cis-trans isomer ratio in secondary amides. They noted that with an increase in solvent polarity there was an increase in the rotational barrier.

If there are cations present in the solvent this too increases the rotational barrier for they become bonded to the oxygen atom. This causes an increase in the C-O bond length and a decrease in the C-O bond order and an increase in the C-N bond order and rotational

barrier. Protonation studies by Murthy, et al.,[31] showed that the rotation barrier of the C-N bond in N-methylacetamide was 36 kcal/mol when protonated and 21 kcal/mol when not protonated. Rode and Fussenegger[32] have done studies on the effect of cations on the rotation barrier and found that as there was an increase in the $[Li^+]$ there was an increase in the rotation barrier.

A considerable amount of work has been done on steric effects and rotation barrier energy of the C-N bond, most of which have resulted from nmr studies and EHT and CNDO/2 calculations.[33-36] The conclusions from each of these investigations indicated that as there was an increase in the size of the substituents R, R', and/or R" in the amide there was a decrease in the rotational barrier height of the amide bond. Representative examples of data for a series of N, N-dimethylamides, $RCON(CH_3)_2$, show a change in barrier height from 18 kcal/mol for R = Me to 11 kcal/mol for R = t-Bu.[33]

From the above discussion one can conclude that the electronic effects due to substituents and solvents as well as steric effects due to the size of R and R' play an important role in determining the rotational barrier height. In view of the present work on the N-chloro-N-substituted amides it was possible that the electronegative chlorine could withdraw a substantial amount of the electron density on the nitrogen and thus diminish the double bond character and decrease the rotational barrier energy. From CNDO calculations by Rao[37] on N-chloracetamide in both the trans and cis form he found the mobile bond order to be 0.4889. It seems logical to assume that by substituting an electron donating group for the hydrogen on the nitrogen this would cause a slight increase in the bond order. Thus one may conclude

that the mobile bond order would be slightly higher than 0.4889 for these amides.

To determine whether the rate was dependent on inductive or steric effects alone or on both steric and inductive effects a multiple regression analysis was performed on part of the data. The results from this analysis as presented in Table IV indicate that the best correlation exists when inductive effects are omitted. It was noted that the value for N-chloro-N-methylacetamide seemed out of line, so a second set of the analyses was performed with the value for N-chloro-N-methylacetamide being deleted. In each instance a higher correlation coefficient was obtained, with the optimum r value being obtained by deleting the N-chloro-N-methylacetamide and the inductive effects. Even so, this correlation yielded only r = 0.820 indicating considerable scatter of the data about the regression line.

This analysis suggested that the rate differences were due mainly to steric effects. While it has been shown that increasing the bulkiness of the R-groups does lower the rotational barrier height and seemingly would increase the rate of abstraction it is also possible that relief of steric hindrance during formation of the amido radical could be directly related to the increase in the rate of abstraction. INDO calculations[10] on the formamido radical concerning the energy dependence of the π and Σ_N electronic ground states on the CNX angle (θ) showed that the energy minima for the ground state of the π radical existed at $\theta = 115^{\circ}$ while for the Σ_N ground state the energy minima existed at $\theta = 180^{\circ}$. The same calculations performed on the N-methylformamido radical showed that the energy minima for both the π and Σ_N electronic ground states was near $\theta = 180^{\circ}$. This suggested

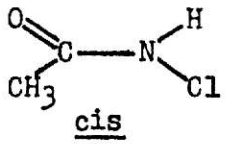
the existence of steric strain in the amide being caused by the presence of the methyl group. Therefore, as larger groups are substituted on the nitrogen this would allow for a relatively easy distortion of the CNX angle and thus allow θ to increase. This tendency to "open up" and relieve the steric strain would supply an added driving force for the amido radical formation and hence increase the rate of formation. In order to determine whether it was the rotational barrier height or the relief of steric strain involved, an attempt was made to obtain a relative estimate of the rotational barrier heights of several representative N-chloramides.

Since the rotational barrier height is directly dependent on the C-N double bond character, it was thought that this could be determined indirectly from the recorded C=O stretching frequency. This stretching frequency is dependent on the amount of C=O double bond character. The greater the C=O double bond character is, the less will be the C-N double bond character and the rotation barrier.

From the results as shown in Table V one is led to the conclusion that there is no significant difference in the rotation barrier. This is obviously incorrect since it has been shown in other studies[33-36] that larger and bulkier groups do lower the rotation barrier. This method therefore could not be used to determine relative rotational barrier heights. The conclusion remains that it is very probable that the steric effects do lower the rotation barrier, and hence, allow for an increase in the rate of abstraction.

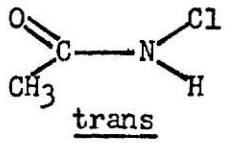
The other plausible explanation of steric effects would be that of the relief of steric strain. Amides are planar about the amide

bond and exist in two isomeric forms, cis and trans. It has been determined by Rao, et al.,[37] using infrared spectroscopy that the ratio of cis (54) to trans (55) in N-chloracetamide is 33:67. No



cis

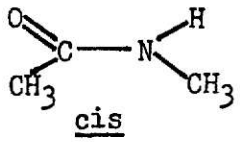
(54)



trans

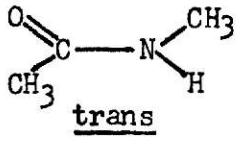
(55)

explanation was offered but the reason could be that the radius of oxygen is smaller than that of the methyl group and hence there is less steric hindrance in the trans form. Infrared studies[30] on conformations of secondary amides show that the cis (56) to trans (57) ratio of N-methylacetamide is 0:100, again suggesting that the oxygen



cis

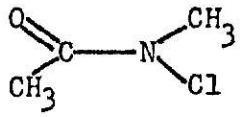
(56)



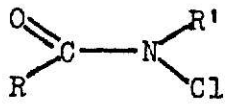
trans

(57)

has a smaller radius than the methyl group so there is less steric hindrance in the trans position. Other conformation studies[38] support the same conclusion that the trans conformation is strongly preferred in N-monosubstituted amides and that in N, N-disubstituted amides the bulkier group is preferred to be cis to the oxygen. There have been no recorded isomeric ratios of N-chloro-N-substituted amides. It is logical to assume that since the Van der Waals radius for CH_3 (2.0 Å)[25] is larger than for Cl (1.8 Å)[25] it would adopt the trans position (58). Such would also be the predominant isomer (59) as R and/or R' increases in size. If the amide possesses a planar structure and has considerable



(58)



(59)

amount of double bond character then an increase in the size of R' would cause an increase in steric strain. The removal of the chlorine would cause a considerable decrease in the strain by allowing the molecule to open up (eq. 60). This effect was predicted by Koenig, et al.[10]

(60) 

From the data in Table II the results for N-chloro-N-methylacetamide seem out of line for it should have the slowest rate if steric effects were the important rate-determining factor. In performing the multiple regression analysis it became evident that by deleting the value for N-chloro-N-methylacetamide a much better correlation was obtained. These results indicated something peculiarly different about this N-chloramide. An investigation of the nmr spectra of reaction products which will be discussed in the Products section showed that the parent amide was not formed for either N-chloro-N-methylacetamide or the other N-chloramides where nitrogen was bonded to a primary carbon in the alkyl substituent. At first this did not seem unusual because the α-hydrogens of the amido radical could allow for facile secondary reactions of the radical in addition to simple abstraction of hydrogen. Further speculation on this problem led to the possibility of the parent

amide being chlorinated by the N-chloramide present in competition as discussed above. This could be particularly true in a reaction mixture such as N-chloro-N-methylacetamide and N-chloro-N-tert-butylacetamide. N-tert-Butylacetamide would be relatively difficult to chlorinate by N-chloro-N-methylacetamide because of the steric hindrance due to the t-butyl group. However the reverse reaction (eq. 61) could take place quite readily. If this reaction (eq. 61) did

(61) $CH_3-\overset{O}{\overset{\|}{C}}-\underset{Cl}{N}-C(CH_3)_3 + CH_3-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-CH_3 \longrightarrow CH_3-\overset{O}{\overset{\|}{C}}-\underset{Cl}{N}-CH_3 + CH_3-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-C(CH_3)_3$

occur to any significant extent it would cast doubt on the validity of all the relative rate constants determined prior to this point.

The results in Table VI do show that this type of reaction (eq. 61) does exist in the absence of PAT and hence, could have a significant effect on the observed rate of chlorine abstraction by the phenyl radical. By assuming $K_{eq} = 10$ and performing the appropriate calculations whereby the initial concentration ratio of the N-chloramides was varied, it was found that this caused a significant change in the k_A/k_B ratio. This result supported the fact that such an equilibrium reaction as shown by equation (61) did not affect the observed relative rate since it had been shown previously that the relative rate value was insensitive to the ratio of the competing N-chloramides. From this result one can conclude that at least where the K_{eq} would be large the relative rate values would not be significantly affected by this equilibrium process.

In the case of where K_{eq} is small if both N-chloramides are present in the reaction products mixture as in reactions where R' = Me

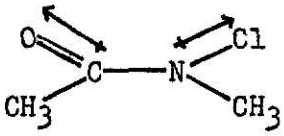
vs. R" = Et or n-Pr the respective parent amides would also have to be present if such an equilibrium existed. Investigation of the nmr spectra of reaction products gave no indication of either parent amide being present though considerable amounts of both N-chloramides were present. Therefore it may be concluded that such an equilibrium process did not occur to any significant extent in these reactions of the N-chloramides with PAT.

Since this possible equilibrium reaction as well as the steric effects fail to offer an explanation for the larger rate of chlorine abstraction from N-chloro-N-methylacetamide than anticipated in this series of N-chloramides perhaps the explanation lies in a unique conformational difference. Although it was found by Rao, et al.,[30] that N-methylacetamide existed solely as the trans isomer (57), in the present study it was discovered by nmr that there was ca. 50:50 cis-trans ratio of N-methylacetamide in both carbon tetrachloride and benzene solvents. In order to find an answer to this descrepancy nmr spectra were recorded using different concentrations of the amide in carbon tetrachloride as well as using deuterated water to determine whether the N-methyl peak was a doublet caused by the N-hydrogen. These results all gave evidence of ca.50:50 isomer ratio. A nmr spectrum of the amide in chloroform was also recorded since that was the solvent used by Rao, et al.,[30] again the results indicated ca.50:50 ratio. Though an answer to these conflicting results was not found it was thought that sufficient data was obtained to substantiate the 50:50 cis-trans ratio.

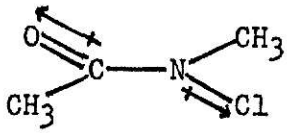
The nmr spectra of the other N-monosubstituted amides that were to be chlorinated gave no evidence of the existence of two isomers,

and likewise there was no such evidence of two isomers existing in any of the N-chloro-N-substituted amides used in this study. From these facts one could conclude that there could be a significant amount of the cis isomer of N-chloro-N-methylacetamide present though it may not be detectable on the nmr time scale.

The chlorine in the cis isomer (62) could conceivably be more easily abstracted. In the trans isomer (63) the two main dipoles oppose each other while in the cis isomer the negative areas of both



(62)



(63)

dipoles lie in close proximity and tend to repel each other. This dipole repulsion could be a significant driving force for the chlorine abstraction process and formation of the amido radicalwhich would result in a faster rate of chlorine abstraction than anticipated for steric effects alone. If the existence of the cis isomer in the other N-chloramides was not of any significance then their relative rates would be mainly dependent on steric effects.

Other possible explanations for the unique position of the rate of chlorine abstraction from N-chloro-N-methylacetamide could be the relative ease of α-hydrogen abstraction by phenyl or other radicals present thus causing an elimination of chlorine. Or, perhaps, the chlorine abstraction process for N-chloro-N-methylacetamide is unique and proceeds via a different reaction pathway with a different rate determining step. The discussion of this matter still remains speculative as no direct evidence was found to offer a more conclusive

explanation.

In summary from this study of the kinetics of chlorine abstraction one may conclude that the rate is dependent mainly on steric effects introduced by the R and R' groups. The steric effects could act by reducing the rotational barrier height thus increasing the probability for a less sterically hindered approach of the phenyl radical as well as increasing the potential of forming the π amido radical. The other possible result of the steric effects is the relief of steric strain in the formation of the amido radical. It may also be concluded from the kinetics part of this investigation that there was no evidence of a concerted β-scission even in the most favorable instance (eq. 29) where an -enedione and a stabilized benzyl radical would have been formed.

It became increasingly apparent as these studies progressed, that the determination of relative rate constants for chlorine abstraction from N-chloramides was more complicated than previous halogen abstraction studies conducted in this laboratory. Unlike relatively inert aromatic and aliphatic halides, N-chloramides are reactive compounds and prone to various reaction and decomposition pathways. Nonetheless, in spite of the difficulties encountered, it is believed that adequate control experiments have been conducted to validate the relative rate constants and other conclusions arrived at in this thesis.

III. NMR Investigations of PAT Reaction Products

A. Results

The relative rates show that a concerted β-scission probably does not occur but this does not exclude β-scission as a subsequent reaction of the amido radical. The second part of the study was to probe whether such a β-scission is a significant reaction of the amido radical. As mentioned earlier this may be of importance in relation to protein degradation. Hydrolysis of the imine or the isocyanate product would actually cleave the peptide chain. This part of the study dealt with an investigation of the nmr spectra of the products from the reactions of N-chloramides with PAT.

An investigation of the nmr spectra indicated considerable amounts of the parent amide being formed in some of the reactions. Table VIII shows an approximate per cent yield of the parent amide formed as determined by a comparison of peak heights on the nmr spectra. In some cases the spectrum was too complex to determine whether the parent amide was present.

To investigate the efficiency of chlorine abstraction by the phenyl radical in this series of N-chloramides a glc analysis was run on the reaction products to determine the amount of chlorobenzene present. The per cent chlorobenzene formed relative to the amount of PAT is shown in Table IX.

To check on the significance of any secondary reactions involved in the formation of the amido radical the ratio of total amount of reacted N-chloramide to PAT was calculated (eq. 64). This value should

Table VIII

Per Cent of Parent Amide Formed in Competitive PAT - N-Chloramide Reactions Indicated in Table II

Amide: RCONHR'		Per cent
R	R'	
CH_3	CH_3	0
CH_3	CH_2CH_3	0
CH_3	$CH_2CH_2CH_3$	0
CH_3	$CH(CH_3)_2$	uncertain[a]
CH_3	CH_2CH_2Ph	5
CH_3	$CH_2C(CH_3)_3$	uncertain[a]
CH_3	$C(CH_3)_3$	25-50[b]
CH_3	$C(CH_3)_2CH_2Ph$	25
CH_3	$C(CH_3)_2Ph$	25
CH_3	$C(CH_3)(COOCH_3)CH_2Ph$	0
Ph	$C(CH_3)_3$	30
$PhCH_2$	$C(CH_3)_3$	30
Amine		
2,2,6,6-tetramethylpiperidine		17

a The spectrum was too complex for the identification of the parent amide.

b The N-chloramide was used with six different amides and the per cent of this parent amide formed varied according to the other N-chloramide present.

(64) $$\frac{\Delta[A] + \Delta[B]}{[PAT]_o} = 1.00 \qquad \begin{aligned} [A]_t - [A]_o &= \Delta[A] \\ [B]_t - [B]_o &= \Delta[B] \end{aligned}$$

be equal to 1.00 if all the phenyl radicals and only the phenyl radicals abstracted the chlorine. These ratios are included in Table IX.

Table IX

Per cent of Chlorobenzene Formed Relative to PAT and the Ratio of Reacted N-Chloramide to PAT

R	Amide: RCONClR' R'	$\frac{C_6H_5Cl}{PAT}$ [a]	$\frac{Amide}{PAT}$ [a]
CH_3	CH_2CH_3	45	0.85
CH_3	$CH_2CH_2CH_3$	49	1.04
CH_3	CH_2CH_2Ph	35	1.03
CH_3	$CH(CH_3)_2$	32	0.76
CH_3	$CH_2C(CH_3)_3$	48	1.08
CH_3	$C(CH_3)_3$	48	1.15
CH_3	$C(CH_3)(COOCH_3)CH_2Ph$	51	0.99
$PhCH_2$	$C(CH_3)_3$	56	1.12
Ph	$C(CH_3)_3$	61	1.13
	Amine		
N-chloro-2,2,6,6-tetramethyl-piperidine		45	0.80

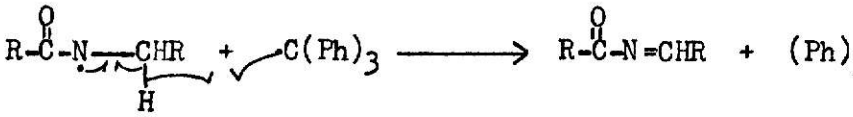
[a] These values resulted from competitive reactions of the indicated N-chloramides and N-chloro-N-methyl-acetamide.

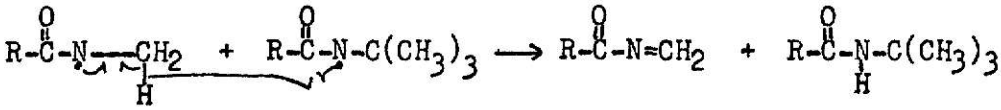
B. Discussion

The most plausible reactions of the amido radicals formed in this study would be coupling with trityl radicals, intermolecular abstractions of hydrogen and/or chlorine, dimerization, disproportionation, or β-scission of either a C-H or C-C bond. In competitive kinetic studies of hydrogen abstraction from RH in CCl_4, Bridger and Russell[39] used PAT as the source of phenyl radicals and found that the trityl radical was quite efficient in scavenging R· and $\cdot CCl_3$ thus preventing secondary reactions and chain processes from occurring. Therefore, it seems likely that a large amount of the amido radical formed in the present study coupled with trityl radicals. Intermolecular hydrogen abstraction would most likely occur from the amides or from solvent-derived intermediates. Direct abstraction of hydrogen from the benzene solvent is unlikely.[3] Intramolecular abstractions likewise are not very likely because this has been shown to occur mainly from the C-4 position and such a position doesn't exist in the amides chosen for the present study. In view of the numerous possible reaction pathways and the resulting complex nmr spectra, only selected reaction products were looked for, namely the parent amide and the more probable β-elimination products.

The nmr spectra gave considerable evidence of parent amide formation as shown in Table VIII. In most instances when the R and/or R' groups were bulky there was from 25-30% formation of the parent amide. The results showed that in every case where α-hydrogens were present there was little or no parent amide formed. This could be evidence of a significant amido radical reaction whereby the α-hydrogen was readily

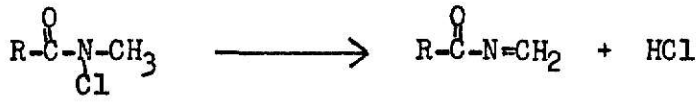
abstracted by other radicals present including the trityl radical (eq. 65). But it also suggests that a radical-radical disproportionation could have taken place with available α-hydrogens (eq. 66).

(65) 

(66) 

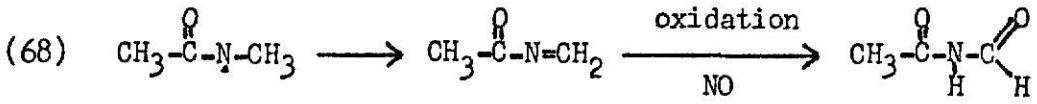
This type of reaction would be particularly favored when one amido radical has α-hydrogens and the other has a tertiary carbon bonded to the nitrogen. This situation would exist in competitive reactions where R' = Me and R" = t-Bu. This offers an explanation as to why there is little or no parent amide formed when α-hydrogens are present and considerable parent amide formed when α-hydrogens are absent.

In photolysis work on rearrangements in the N-halamides[9] it was pointed out that the reason for a low yield of N-methylchloramide rearrangements was possibly due to the heightened activity of the α-hydrogens and the probable dehydrohalogenation reaction (eq. 67).

(67) 

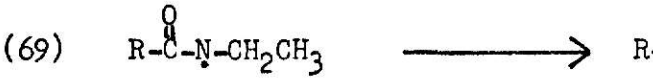
Chow and Tam's study of amido radical reactions,[40] using the N-nitrosamides, showed that elimination of the α-hydrogen is a significant reaction. They also showed that this is dependent on the solvent and was increasingly favored as the solvent is changed from mesitylene to cyclohexane to benzene. In the photolysis of N-nitroso-N-methylacet-

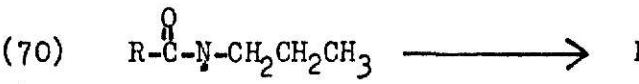
amide in benzene they recorded 38% of the parent amide and 27% of N-formylacetamide (eq. 68). The latter was formed from oxidation of N-methyleneacetamide.

(68) 

Although the α-hydrogens can be readily abstracted from the amido radical, thus eliminating the possibility of parent amide formation, there is another explanation for the absence of these parent amides. This explanation follows from a final control used to check the relative rate constants, that of a parent amide being chlorinated by an N-chloramide (eq. 45). From the results of these reactions as shown in Table VI it is evident that where R' = Me or Et the amide can be readily chlorinated. If R' is larger, such as t-Bu, the amide can not be readily chlorinated but the N-chloramide can act as a good chlorinating agent. Even though it was determined that this chlorination reaction didn't have significant effect on the relative rate constants, it does offer an explanation for the absence of parent amides containing α-hydrogens particularly in reactions of R' = Me vs. R" = t-Bu or other large groups.

There are several products possible from β-elimination involving the alkyl portion of the amido radical (eq. 69-77). Another type of

(69) 

(70) 

(71) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-CH(CH_3)_2 \longrightarrow R-\overset{O}{\overset{\|}{C}}-N=CH(CH_3) + \cdot CH_3$

(72) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-C(CH_3)_3 \longrightarrow R-\overset{O}{\overset{\|}{C}}-N=C(CH_3)_2 + \cdot CH_3$

(73) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-CH_2C(CH_3)_3 \longrightarrow R-\overset{O}{\overset{\|}{C}}-N=CH_2 + \cdot C(CH_3)_3$

(74) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-CH_2CH_2Ph \longrightarrow R-\overset{O}{\overset{\|}{C}}-N=CH_2 + Ph\dot{C}H_2$

(75) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-C(CH_3)_2Ph \longrightarrow R-\overset{O}{\overset{\|}{C}}-N=C(CH_3)Ph + \cdot CH_3$

(76) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-C(CH_3)_2CH_2Ph \longrightarrow R-\overset{O}{\overset{\|}{C}}-N=C(CH_3)_2 + Ph\dot{C}H_2$

(77) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-C(CH_3)(COOCH_3)CH_2Ph \longrightarrow R-\overset{O}{\overset{\|}{C}}-N=C(CH_3)(COOCH_3) + Ph\dot{C}H_2$

β-elimination could occur that would result in the formation of isocyanates (eq. 78). Beckwith and Goodrich,[8] in their work on free radical rearrangements of N-chloramides stated that products from side reactions showed formation of isocyanates.

(78) $R-\overset{O}{\overset{\|}{C}}-\dot{N}-R' \longrightarrow R\cdot + O=C=N-R' \qquad R\cdot = \dot{C}H_3,\ Ph\dot{C}H_2,\ Ph\cdot$

The above illustrations are possibilities of β-elimination products. If such an elimination did occur the new radical formed would be free to abstract chlorine from an N-chloramide. The most probable β-elimination product would be the stabilized benzyl radical (eqs. 74, 76, 77) which could abstract either chlorine or hydrogen

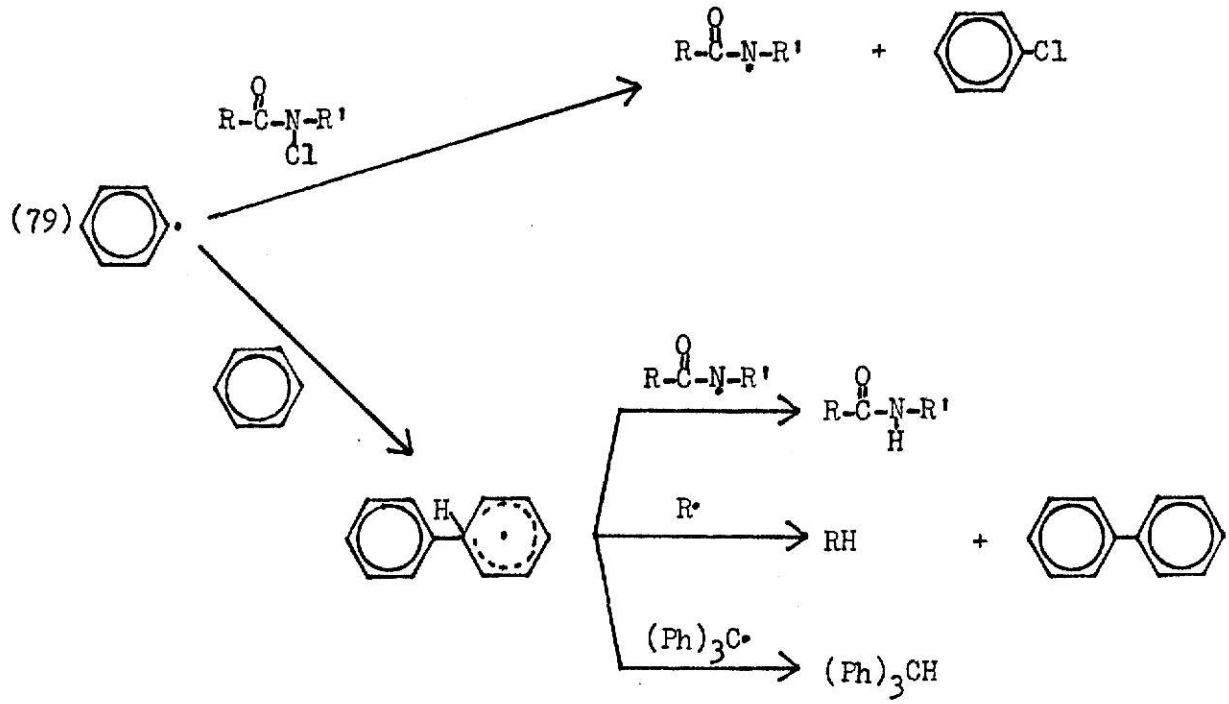
forming benzyl chloride or toluene. The nmr spectra gave no evidence of either being formed, not even from N-chloro-N-(1-methyl-1-benzyl methyl acetate)acetamide (eq. 77) which represents the most favorable case. It may therefore be concluded from an investigation of the nmr spectra of reaction products that β-elimination did not occur to any significant extent in these amido radical reactions.

Using a glc analysis on the reaction products to determine the per cent of the phenyl radical that abstracted the chlorine showed that, on the average, 40-46% of the theoretical yield of chlorobenzene was formed (Table IX). The ratio of the total amount of the reacted amide to PAT consumed should be equal to 1.00 (eq. 64) if the rate of the reaction is dependent only on the phenyl radical abstraction of chlorine. Examination of Table IX reveals that this value is approached for most of the reactions but that the ratio varied from 0.76 to 1.15. Considering on the average that only 50% of the phenyl radicals abstracted the chlorine, then the actual ratio of total amide decomposed to PAT consumed should be about 0.5. Since the ratio is closer to 1.0 and all the PAT is decomposed, there appear to be some secondary reactions responsible for the remainder of the amide decomposition.

Bridger and Russell[39] used PAT as the source of the phenyl radical in measuring rates of hydrogen and chlorine abstraction from solvents RH and CCl_4. They found that, on the average, the total yields in the RH/CCl_4 mixtures were 70-80% benzene and chlorobenzene. In pure CCl_4 they found that there was ca. 5% benzene formed due to the phenyl radical abstraction of hydrogen from the PAT molecule.

From their results it may be concluded that PAT does not have 100% efficiency in hydrogen and chlorine abstraction. They used a

small ratio of PAT to solvent, 0.091 mol/l. In the present work a much larger ratio of PAT to amide was used but this was diluted in the benzene solvent. A typical amount used was 0.50 mmol of the amide mixture, 0.25mmol of PAT and 11 mmol of benzene. Therefore the addition reaction of the phenyl radical to benzene is probably significant. Since solvent is present in a large amount compared to the amount of N-chloramides, it is probable that a significant fraction of phenyl radicals added to the solvent to form a complex with a readily abstractable hydrogen (eq. 79). This hydrogen could easily be abstracted by any radical present and, if the abstracting radical were amido, this would account for the relatively large amounts of parent amide produced.

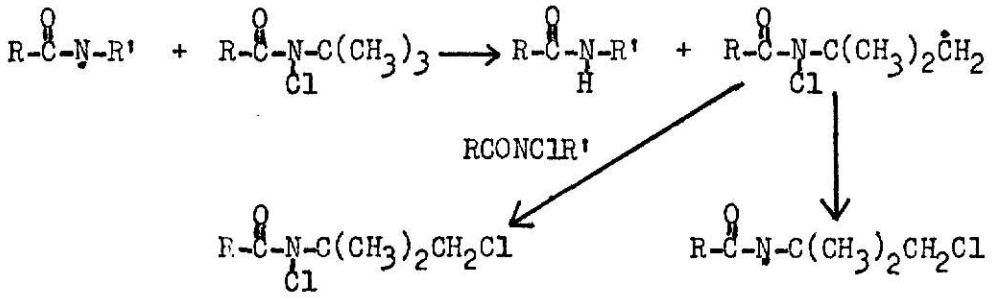


If HCl were generated to any significant extent, this would offer an explanation for the relatively low yield of chlorobenzene. It has been shown above that HCl reacts with N-chloramides to form molecular

chlorine and the parent amide[23] (eq. 42-44). The addition of a base to neutralize the HCl formed should change the reaction rate since N-chloramide would be expected to be consumed rather indiscriminately. Addition of excess Na_2CO_3 to three different ampoules of N-chloro-N-methylacetamide and N-chloro-N-tert-butylacetamide before reaction gave no evidence of change in the relative reaction rate beyond the usual experimental error. Therefore one is led to conclude that HCl is not formed to any significant extent.

Another explanation of the low yield of chlorobenzene compared to the amount of chlorine abstraction would be that of intermolecular and possibly intramolecular chlorine abstraction (eq. 80). Other

(80)



chlorine abstraction pathways might involve trityl radicals or the radicals formed from the many amido radical decomposition products. There was no evidence for N-chloramide consumption by processes other than radical abstraction, although it probably cannot be unequivocally stated that phenyl radicals only were involved in the abstraction reaction.

IV. Phenyl Radicals from Benzoyl Peroxide Reacting with a Single N-Chloramide

A. Results

In order to study reactions of the amido radical further, a second halogen abstraction method was used to generate the amido radical. In this case only a single N-chloramide was subjected to phenyl radical attack, the phenyl radical being produced by thermal decomposition of benzoyl peroxide. Four N-chloramides in amounts varying from 0.4 to 0.7 mmol were allowed to react separately with 0.1 mmol of benzoyl peroxide in benzene in the dark for 5 hours at 100°C. The results from an analysis of the nmr spectra as shown in Table X indicated no N-chloramide remaining. Since there should have been a considerable amount of this remaining, this indicates that an important secondary reaction occurred to decompose the N-chloramide.

B. Discussion

From a study of the nmr spectra of the reaction products in the N-chloramide reactions with PAT there existed no evidence for β-scission. The main emphasis in those studies was one of kinetics and not one involving an identification of reaction products. With two amides breaking down via radical reactions the nmr spectra became too complex and not conducive to giving positive evidence of certain types of reactions.

Because of the complexity of the PAT reactions several of the N-chloramides were submitted to a phenyl radical attack from another source, benzoyl peroxide (eq. 81). The reaction ampoules were pre-

Table X

Chemical Shifts[a] Resulting from the Benzoyl Peroxide Reaction with N-Chloramides

N-Chloramide	Reference[b]	Control[c]	Peroxide[d]
$CH_3CONClCH_3$	singlet 1.80 singlet 2.90	singlet 1.80 singlet 2.90	singlet 9.70 multiplet 1.20 multiplet 1.80
$CH_3CONClC(CH_3)_3$	singlet 1.40 singlet 2.00	singlet 1.40 singlet 2.00	singlet 1.20 singlet 1.70 singlet 1.55 singlet 2.45 singlet 4.05
$CH_3CONClCH_2CH_2Ph$	singlet 1.80 triplet 2.75 triplet 3.70	singlet 1.60 multiplet 2.60 multiplet 3.30	singlet 1.90 multiplet 1.75 multiplet 2.80 multiplet 3.40
$CH_3CONClC(CH_3)_2CH_2Ph$	singlet 1.40 singlet 2.00 singlet 3.20	singlet 1.20 singlet 1.40 singlet 1.60 singlet 2.00 singlet 3.10 singlet 3.20	singlet 0.90 singlet 1.20 singlet 1.50 singlet 1.70 singlet 2.40 singlet 3.10

[a] The chemical shifts are recorded in δ with reference to TMS.

[b] The nmr spectra as recorded in benzene.

[c] The N-chloramide heated at 100°C for 5 hours without benzoyl peroxide.

[d] The N-chloramide heated at 100°C for 5 hours with benzoyl peroxide.

pared in the same manner as those containing PAT and using approxi-

(81) $$Ph\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}O\text{-}\overset{O}{\overset{\|}{C}}\text{-}Ph \xrightarrow{100^\circ} Ph\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\cdot \longrightarrow Ph\cdot + CO_2$$

mately the same ratios of phenyl radical to N-chloramide in benzene

solvent. The major difference was that these solutions were heated at 100°C for 5 hours to insure complete breakdown of the peroxide and formation of the phenyl radicals. Two amides used were of low potential for β-scission, N-chloro-N-methylacetamide and N-chloro-N-tert-butylacetamide, and two of higher potential for β-scission, N-chloro-N-phenethylacetamide and N-chloro-N-(1,1-dimethyl-2-phenethyl)acetamide.

If there were any significant amount of β-scission in these reactions, formation of the stabilized benzyl radical from the latter two compounds would be anticipated. This radical could abstract either chlorine or hydrogen and form either benzyl chloride or toluene. The nmr spectra showed that neither of these was formed, suggesting that this was probably not a significant reaction pathway.

However, the results of N-chloro-N-phenethylacetamide must be viewed with some caution because this amide completely decomposed on heating at 100° without peroxide. Likewise a small amount of N-chloro-N-(1,1-dimethyl-2-phenethyl)acetamide was partially decomposed under the same conditions. With the peroxide present however, the latter amide was completely reacted.

In the case of both these amides, if one allows for a shift downfield (0.4 ppm and 0.2 ppm respectively) of the methyl attached to the carbonyl carbon due to the presence of HCl, then the major product in each reaction is the parent amide. The HCl which reacts with the N-chloramide to form the parent amide could be formed as a result of the high-temperature conditions causing a cleavage of the N-Cl bond. This fact will be further discussed in the photolysis section.

Neither N-chloro-N-methylacetamide nor N-chloro-N-tert-butyl-

acetamide was affected by high temperature. After reaction with peroxide neither showed the presence of any unreacted N-chloramide. N-Chloro-N-tert-butylacetamide showed a considerable amount of the parent amide. N-Chloro-N-methylacetamide showed none of the parent amide which is evidence favoring α-hydrogen abstraction.

Since none of the N-chloramide remained in these reactions with benzoyl peroxide and the ratios of the phenyl radical to amide ranged from 1:2 to 1:3, another significant reaction must be occurring that causes the decomposition of the remainder of the N-chloramide. This could be due either to thermolysis, which is aided by the radical initiation reactions, or to the presence of acid. Because of the inconclusiveness of these results, this method of studying the amido radical reactions was discontinued.

V. Photolytic Generation of Amido Radicals

A. Results

A third method of amido radical production was employed to further investigate the amido radical reactions, that of photolysis. N-Chloro-N-phenethylacetamide was exposed to ultraviolet radiation from a 275 watt sunlamp source for a one-hour period to determine whether β-scission was a significant decomposition pathway. Six solvents were used with the results presented in Table XI.

Although β-scission to form toluene (2.32% in CCl_4 and 2.07% in C_6H_6) or benzyl chloride (4.49% in CCl_4 and 4.02% in C_6H_6) was not evident from the results of Table XI, it was evident that some type of chemical reaction had occurred. A second set of photolytic reactions

Table XI

Respective Chemical Shifts[a] Resulting from Photolysis of N-Chloro-N-phenethylacetamide

Solvent		singlet $\underline{CH_3}$-	triplet -N-$\underline{CH_2}$	triplet -$\underline{CH_2}$-Ph	singlet $\underline{Ph}$	other peaks
CCl_4	before hν	2.10	3.80	2.85	7.10	
	after hν	1.95	3.40	2.80	7.10	1.90 2.00 7.25
$CHCl_3$	before hν	2.10	3.90	2.95	7.20	7.27
	after hν	2.20	3.55	2.90	7.20	2.05 2.10 7.27
Dioxane	before hν	2.00	3.90	2.90	7.20	
	after hν	2.25	3.75	2.90	7.20	
C_6H_6	before hν	1.80	3.70	2.80	7.10	
	after hν	1.95	3.50	2.85		
CH_3OH	before hν	1.95	3.90	2.95	7.20	3.35 4.75
	after hν	2.20	3.60	2.90	7.20	3.35 3.67 4.50 5.80
CD_3COCD_3	before hν	2.00	3.90	2.95	7.20	
	after hν	2.00	3.45	2.80	7.20	2.00 7.40

[a] Chemical shifts are recorded in δ with reference to TMS.

was run on N-chloro-N-tert-butylacetamide with results recorded in Table XII. Results of further treatment of the irradiated N-chloro-N-tert-butylacetamide in dioxane are recorded in Table XIII.

The photolysis results as recorded in Table XIII seemed to indicate that the parent amide was being formed and the HCl also produced

Table XII

Respective Chemical Shifts[a] Resulting from Photolysis of N-Chloro-N-tert-butylacetamide

Solvent		singlet CH_3	singlet $C(CH_3)_3$	other peaks
Dioxane	before hν	2.15	1.40	1.25, 1.75
	after hν	2.40	1.40	
CH_3OH	before hν	2.20	1.45	3.35, 4.65 ($\underline{CH_3OH}$)
	after hν	2.30	1.40	3.35, 6.25 ($\underline{CH_3OH}$)
				3.65, 4.50
CCl_4	before hν	2.20	1.45	
	after hν	2.20	1.45	1.25, 1.35, 1.55, 1.85, 1.90, 2.25, 3.80, 3.90, 6.60, 6.80

[a] Chemical shifts are recorded in δ with reference to TMS.

Table XIII

Chemical Shifts[a] Resulting from Variations in the Photolysis of N-Chloro-N-tert-butylacetamide

Treatment	CH_3	$C(CH_3)_3$	other peaks
Control, before hν	2.15	1.45	
after hν	2.40	1.40	
Degassed, before hν	2.15	1.45	
after hν	2.40	1.40	
Control, after hν degassed	2.30	1.40	7.65
Control, after hν heated	2.30	1.40	6.70
Control, after hν addition of NaOD	1.90	1.30	white ppt.

[a] Chemical shifts are recorded in δ with reference to TMS in dioxane.

caused the respective chemical shifts. If the amount of change in the chemical shift is dependent on the amount of HCl present, then this change should be detectable in a time-monitored irradiation procedure. Therefore an nmr spectrum was recorded for each of the irradiated solutions at the different time intervals listed in Table XIV.

Table XIV

Chemical Shifts[a] of the CH_3 Attached to the Carbonyl Carbon with Timed Exposures in Dioxane

N-Chloramide	0 min	5 min	10 min	15 min	20 min	30 min
$CH_3CONClCH_2CH_2Ph$	2.00	2.00	2.00	-	2.25	2.30
$CH_3CONClC(CH_3)_3$	2.20	2.20	2.20	2.35	2.40	2.45
$CH_3CONClCH_2C(CH_3)_3$	2.20	2.00	2.35	-	2.40	2.50

[a] Chemical shifts are recorded in δ with reference to TMS.

To confirm the fact that the shifts indicated in Tables XIII and XIV are due to the presence of HCl, dry HCl gas was bubbled into N-chloro-N-tert-butylacetamide and N-tert-butylacetamide. This produced the respective chemical shifts recorded in Table XV.

From a study of the results as recorded in Tables XII - XV it became apparent that HCl was being formed and was converting the greater part of the N-chloramide to the parent amide thus not allowing for any significant amount of subsequent amido radical reaction. To inhibit the presumed free radical chain generation of HCl, the photolysis of N-chloro-N-phenethylacetamide was repeated using tri-

Table XV

Chemical Shifts[a] Due to Addition of $HCl_{(g)}$ to N-Chloro-N-tert-butylacetamide and N-tert-Butylacetamide

Amide	Treatment	CH_3	$C(CH_3)_3$	other
$CH_3CONClC(CH_3)_3$	control	2.20	1.45	
	HCl, 10 sec	2.20	1.45	1.30 1.80
$CH_3CONHC(CH_3)_3$	control	1.85	1.30	
	HCl, 1 min	2.20	1.40	
	HCl, 4 min	2.55	1.45	

a Chemical shifts are recorded in δ with reference to TMS in dioxane.

chloroethylene as a chlorine atom trap.[41] Two different sources of ultraviolet radiation were used with the results illustrated in Table XVI. Trichloroethylene apparently served as an efficient trap for chlorine and prevented formation of HCl as is evident by no change in the chemical shift of the parent amide.

Table XVI

Chemical Shifts[a] from Photolysis of N-Chloro-N-phenethylacetamide Using a Chlorine Trap, $CHCl=CCl_2$

Treatment	$\underline{CH_3}$	$-N-\underline{CH_2}-$	$-\underline{CH_2}-Ph$	$\underline{Ph}$	other
Control	2.00	3.80	2.90	7.15	
Sunlamp, 1 hr	2.00	3.80	2.90	7.15	1.90 (small)
ESR lamp, 30 min at -100°C	2.00	3.80	2.90	7.15	1.90 (medium)
ESR lamp, 90 min at 0°C	2.00	3.80	2.90	7.15	1.90 (large)

a Chemical shifts are recorded in δ with reference to TMS in dioxane.

B. Discussion

The purpose of this photolysis section was again to probe whether β-scission occurs from the amido radical. Since both Gellert[14] and West[15] obtained evidence of β-scission in their esr studies of the amido radical, photolysis seemed a good method for further investigation of the amido radical. The amide chosen for this study was N-chloro-N-phenethylacetamide because of its potentially good leaving group, the benzyl radical (eq. 82). The benzyl radical could then abstract a chlorine or hydrogen, forming either benzyl chloride or toluene (eq. 83). Both would be easily detectable by nmr. Though there was evidence of

(82) $$CH_3-\overset{O}{\overset{\|}{C}}-N-CH_2CH_2Ph \longrightarrow CH_3-\overset{O}{\overset{\|}{C}}-N=CH_2 + \dot{C}H_2Ph$$

(83) $$PhCH_2\dot{} \xrightarrow[\text{or solvent}]{CH_3CONClCH_2CH_2Ph} PhCH_2Cl + PhCH_3$$

reaction in each case, there was no evidence of benzyl chloride or toluene being formed.

One major change in each spectrum as indicated in Table XI was the shift of the methyl group attached to the carbonyl carbon. In the CCl_4 solvent this was shifted upfield 0.15 ppm. In deuterated acetone there was no shift of this peak while in the other four solvents it was shifted downfield by 0.2 ppm. The other noticeable shift was that of the methylene group directly bonded to the nitrogen. In deuterated acetone this triplet was shifted downfield by 0.4 ppm while in the other five solvents it was shifted upfield by 0.2 to 0.4 ppm. Another significant shift was that of the methanol OH group. This singlet was shifted downfield by 1.1 ppm.

It has been suggested by Johnson and Green[23] that upon photolysis of the N-chloramides there is the formation of a chlorine atom-HCl chain (eq. 84-86) such that HCl reacts with the N-chloramide to convert

(84) $Cl\cdot + SH \longrightarrow HCl + S\cdot$

(85) $HCl + R\text{-}\overset{\overset{O}{\|}}{C}\text{-}\underset{Cl}{N}\text{-}R' \longrightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}\underset{H}{N}\text{-}R' + Cl_2$

(86) $Cl_2 + S\cdot \longrightarrow SCl + Cl\cdot$

it to the parent amide. This type of chain is possible in $CHCl_3$, CH_3OH and dioxane where labile solvent hydrogens are available. This leads to the conclusion that all the N-chloramide was converted to the parent amide. There could be an excess of H^+ present to protonate the amide and thus cause the characteristic shifts. Protonation of the methanol would also shift the OH singlet downfield.

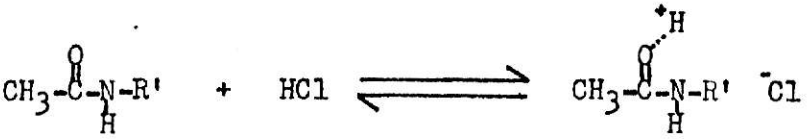
A second set of photolytic reactions was run on N-chloro-N-tert-butylacetamide to determine whether these characteristic shifts would occur in other amides. Using this particular amide the possibility of β-scission occurring in the amido radical was low.

The results with this N-chloramide in CCl_4, as shown in Table XII, were very complex. The major peaks appear to be those of the N-chloramide and the parent amide. In the other two solvents the results are analogous to those of N-chloro-N-phenethylacetamide. The major change in both is a shift of the methyl group bonded to the carbonyl carbon. In CH_3OH this peak was shifted downfield 0.1 ppm and in

dioxane it was shifted downfield 0.2 ppm. The shift of the OH in CH_3OH was 1.6 ppm downfield.

Since none of these tubes had been degassed, it was thought that oxygen could be quenching some radical chain processes. Therefore, a degassed sample of N-chloro-N-tert-butylacetamide in dioxane was irradiated and the nmr spectra showed identical results (Table XIII). If HCl was responsible for the downfield shift of the acyl methyl group, then neutralizing the irradiated sample should cause an upfield shift to occur. Addition of five drops of NaOD to the irradiated tube indeed caused the peak of the acyl methyl to shift upfield to the position of the parent amide, 1.90δ.

In order to determine whether an equilibrium process was established and dependent on the amount of HCl produced, N-chloro-N-phenethylacetamide, N-chloro-N-tert-butylacetamide and N-chloro-N-neopentylacetamide were separately irradiated in dioxane and monitored at the respective time intervals indicated in Table XIV to detect the shifts of the acyl methyl group. The results in Table XIV show with N-chloro-N-tert-butylacetamide and N-chloro-N-phenethylacetamide that no apparent shift of the methyl group had occurred after the first five minutes, but with N-chloro-N-neopentylacetamide there was a shift upfield to the location of the methyl group of the parent amide. At the end of the 10-minute interval the methyl group of each had shifted downfield slightly and by the end of the 20-minute interval each had nearly reached its maximum shift. From these results one can conclude that the parent amide is formed by the chlorine atom-HCl chain (eq. 84-86), and then becomes protonated by HCl produced (eq. 87).

(87) 

To further test this conclusion, HCl gas was bubbled through a solution of N-chloro-N-tert-butylacetamide in dioxane and through a solution of N-tert-butylacetamide in dioxane. The results in Table XV indicate that after 10 sec the nmr spectrum showed half conversion of the N-chloramide to the parent amide. Following 1 min of HCl addition to the parent amide there was a slight shift downfield of the methyl group and at the end of 4 min it had shifted 0.4 ppm downfield. This gives evidence that the parent amide was formed and protonated by HCl.

Since chlorine radicals were the problem in the above attempts to determine whether β-scission occurs in N-chloro-N-phenethylacetamide, it was decided to make one more attempt using the chlorine trap [41] trichloroethylene. With trichloroethylene as the solvent and equivalent amounts of N-chloro-N-phenethylacetamide and dioxane present, the solution was first irradiated for one hour with a 275 watt sunlamp. The nmr spectrum showed a slight change as indicated in Table XVI. It was finally irradiated by a 2000 watt PEK AH6-2B lamp for one hour at 0°C. This caused about 60% of the methyl peak to be shifted upfield 0.1 ppm. This shifted peak corresponded to that of the parent amide. There was no indication of β-scission from the nmr spectra. Therefore, with the chlorine being efficiently trapped, the major product formed was the parent amide.

The results from the investigation of the amido radical being generated by photolysis suggested that the Cl· being formed acted in a chain carrier reaction mechanism causing the formation of the parent

amide via reaction of the N-chloramide and HCl. This conclusion was supported by the amount of change in the nmr chemical shift of the parent amide being dependent on the amount of HCl present. The use of a chlorine trap prevented these characteristic shifts. Since the parent amide was formed in the presence of the chlorine trap it is possible in this case that hydrogen abstraction by the amido radical was occurring. There was no nmr evidence of β-scission taking place in these amido radicals.

VI. Amino Radical Study

To make some comparison of the ease of chlorine abstraction from an amide to that from an amine, N-chloro-2,2,6,6-tetramethylpiperidine was also included in the kinetic studies. Theoretically, the chlorine should be more readily abstracted from the amide. This would be primarily because of the greater N-Cl bond strength in the amine. Also, as mentioned previously in this paper, it has been discussed by Danen[16] that electron-withdrawing groups favor halogen abstraction from organic molecules. In the amide the acyl portion serves as a very efficient electron-withdrawing group. The acyl portion can also provide for the formation of a somewhat resonance stabilized radical. Though N-chloro-2,2,6,6-tetramethylpiperidine may not be a typical amine, it was chosen because of a need for an amine without labile α- or β-hydrogens present.

The calculated relative rate ratio for this reaction with respect to N-chloro-N-methylacetamide was 1.31 (Table II). Although this shows that the chlorine abstraction was slower from the amine than the N-chloro-N-methylacetamide the value is still within the range of relative rate

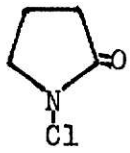
ratios, 0.265 to 2.48, obtained for the N-chloramides. A possible explanation as to why the relative rate ratio value of 1.31 is not considerably larger as anticipated could be due to relief of steric strain in N-chloro-2,2,6,6-tetramethylpiperidine as the radical is formed. This could supply a partial driving force for the chlorine abstraction.

Considering possible products from this reaction one would predict the tetramethylpiperidyl radical to be somewhat stable and not as prone to decomposition as the amido radicals. Hydrogen abstraction would be the more favored subsequent reaction of the amino radical. Roberts and Ingold[42] have shown it to be a fairly reactive radical abstracting hydrogen from toluene considerably easier than the tert-butylperoxy radical. They also stated that the selectivity of this radical is comparable to that of bromine atoms and peroxy radicals even though it forms a much stronger bond to hydrogen.

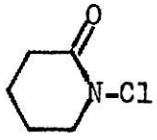
The nmr spectra of the reaction products showed that 29% of the N-chloro-2,2,6,6-tetramethylpiperidine reacted and 17% of the parent amine was produced. This indicated that a significant percentage of the tetramethylpiperidyl radical abstracted hydrogen.

VII. Miscellaneous Studies

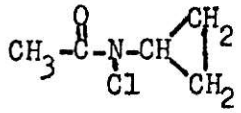
Other N-chloramides synthesized and used in the abstraction reactions but with inconclusive results were N-chloro-2-pyrrolidone (88),N-chloro-2-piperidone (89) and N-chloro-N-cyclopropylacetamide (90). The two cyclic amides were prepared with the intent of observing rotational barrier effects on the rate of abstraction. In both



(88)



(89)



(90)

amides complete rotation about the C-N bond is impossible but a slight twisting out of the amide bond plane is allowed. It was thought that if there were a correlation between the rotational barrier energy and the rate of abstraction, there would be a noticeable change in the rate of chlorine abstraction from these two cyclic amides.

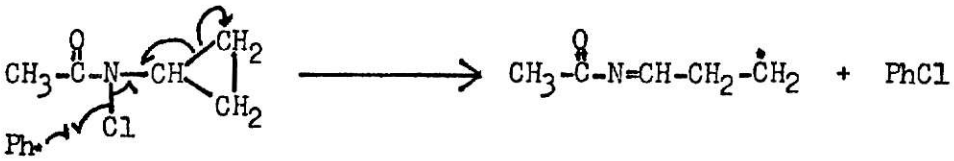
The results obtained, however, could not be used in this study due to the fact that, when a mixture of the cyclic N-chloramide with N-chloro-N-tert-butylacetamide was heated in the sealed ampoule without PAT for four hours, there was considerable reaction of the amides. Inexplicably, each N-chloramide heated alone in a separate ampoule was stable to heat and did not decompose.

The nmr spectra of reaction products gave indication of the major product in each case being the parent amide, N-tert-butylacetamide, with 72% being formed in the N-chloro-2-pyrrolidone reaction and 52% being formed in the N-chloro-2-piperidone reaction. There were no other significant peak changes. In view of the photolysis results it seems as though considerable HCl must have been formed to effect the conversion to the parent amide.

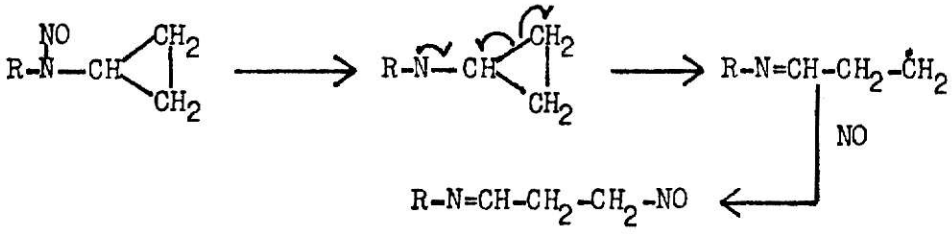
In Gellert's esr studies of amido radicals[14] generated from N-chloro-2-pyrrolidone, N-chloro-5,5-dimethyl-2-pyrrolidone and N-chloro-ε-caprolactam, he was able to detect the homolytic cleavage

of the N-Cl bond by trapping the chlorine. He was not able, however, to observe any of the cyclic amido radicals using several different techniques. This led to the conclusion that, under these conditions, the cyclic amido radical must be extremely reactive.

N-Chloro-N-cyclopropylacetamide was synthesized to be used for the purpose of illustrating the effects of concerted β-scission on the rate of chlorine abstraction. This amide has an excellent potential for concerted β-scission (eq. 91) due to the strained cyclopropyl ring.

(91) 

Dekker, et al.,[43] reported that the photolysis of N-nitroso-N-cyclopropylcarboxamides produced a radical intermediate which reacted with NO (eq. 92). These reactions were carried out in both an inert

(92) 

solvent, $CFCl_3$, and a polar solvent, CH_3OH.

The results of the reactions of both N-chloro-N-tert-butylacetamide and N-chloro-N-methylacetamide with N-chloro-N-cyclopropylacetamide could not be used for the calculation of a rate ratio due to overlap in the nmr spectra. The nmr spectra did reveal, however, that 26% of the N-chloro-N-tert-butylacetamide was converted to the parent amide.

A reaction ampoule of only N-chloro-N-cyclopropylacetamide and PAT in CCl_4 solvent was prepared and allowed to react according to the same conditions. The nmr results of this reaction showed a large peak at 7.2δ. This was chlorobenzene formed by chlorine abstraction from the amide and the solvent. The glc analysis gave 62% of the phenyl radical converted to chlorobenzene. There was a shoulder on the peak at 7.2δ due to benzene being formed thus explaining the remainder of the phenyl radical. There was a small amount of the parent amide formed; and none of the N-chloramide remained.

Due to the fact that there was none of the N-chloramide remaining and only a small amount of the parent amide formed, there must have been extensive decomposition of the cyclopropyl ring. Since there were only two very small unidentified singlets, 2.05δ and 4.20δ, the majority of the decomposition products must have been gaseous or highly volatile at room temperature and escaped during the transfer of the reaction mixture from the ampoule to the nmr tube. Due to the unencouraging and inconclusive nature of the results, the study of this system was not pursued further.

VIII. Experimental

A. General

Nuclear magnetic resonance spectra were obtained using Varian T-60 and XL-100 spectrometers at normal probe temperatures. The nmr spectra of compounds synthesized were recorded using CCl_4 solvent with tetramethylsilane (TMS) as reference for identification. Reaction product mixtures were run in a 5 mm O.D. nmr tube with a coaxial inner

cell containing the internal standard reference. The inner cell has a stem length of 25 mm and a 2 mm O.D. This gave a reference capacity of 10 μl which was submerged in a sample capacity of 339 μl. The internal standard reference used depended on the chemical shifts of the reaction products mixture and was one of the following: dioxane, dimethyl sulfoxide, cyclohexane, or toluene.

Infrared spectra were obtained using Perkin-Elmer Models 137 and 180 infrared spectrometers. Compounds were run in CCl_4 solvent between NaCl plates. The glc determination of chlorobenzene was performed using a Hewlett-Packard F & M Model 700 dual column gas chromatograph utilizing a 6 ft x 1/4 in. SE-30 column.

Melting points were obtained from a Fisher-Johns melting point apparatus. Boiling points were recorded during distillation and were uncorrected.

B. Kinetic Analyses

Reaction ampoules were prepared in the following manner. Two amides in varying ratios of from 0.5 to 1.5 were dissolved in 1.0 ml dry benzene. One-half of this solution was transferred to an ampoule previously dried and containing phenylazotriphenylmethane (PAT). The other half was transferred to a vial and stored under refrigeration for later nmr analysis. The ratio of PAT to total amide was 1:2.

The ampoules containing the reaction mixture were degassed by a freeze-thaw technique at ca. 1 mm pressure using liquid nitrogen for freezing the solution. They were then sealed and placed in an oil bath at 60.0 ± 0.1°C for 4 hours (ca. ten half lives)[39] of PAT.

Following this period of incubation the ampoule mixture was immersed in liquid nitrogen and then placed in a vial and kept under refrigeration for nmr analysis. There were at least four and usually six reaction ampoules prepared and analyzed for the determination of each relative rate ratio recorded in Table II.

The nmr analyses were performed by recording at 250 Hz sweep width a spectrum of the portion of unreacted amide-benzene solution followed by a recording of a spectrum of the product mixture from the reaction ampoule. From the former spectrum initial concentration ratios of reactants were calculated and from the latter spectrum final concentration ratios of reactants were calculated as described on page 12. A peak from each amide, free from overlap and usually a singlet, was chosen for integration. In the recording of each spectrum an internal standard reference was used with a concentration allowing for similar peak height as the amide peaks. Examples of the nmr spectra of a typical run are illustrated in Figures 1 and 2. These spectra show the peaks that were integrated before and after the reaction. Each amide peak and the internal standard peak was integrated 10 times with the average value being used to calculate the concentration ratios of initial and final concentrations of the amide to internal standard thus giving the values for $[A]_o$, $[A]_t$, $[B]_o$ and $[B]_t$ used in the kinetic equation. The multiple regression analysis was run using the MULTREG program available at Kansas State University Computing Center.

Following the nmr analysis of reaction products a known amount by weight of either bromobenzene or iodobenzene was added to the reaction products solution which was analyzed by glc for determination of chlorobenzene present. The area of these peaks was measured by

Figure 1. Partial nmr spectrum before reaction.

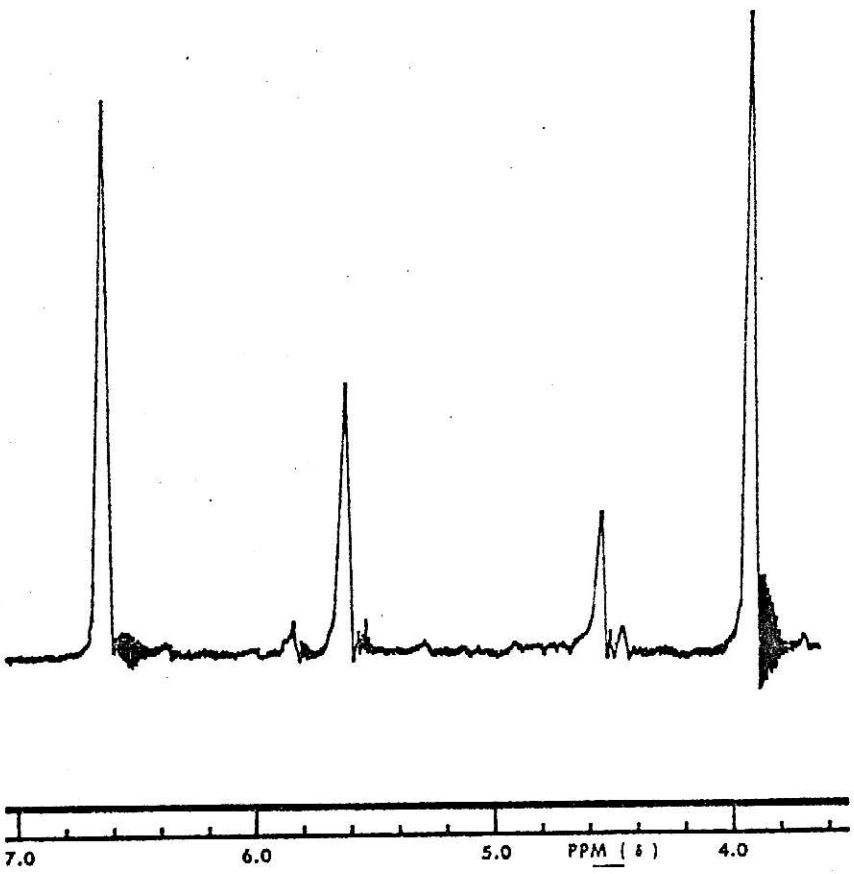


Figure 2. Partial nmr spectrum after reaction.

a An example of a set of peaks used in the determination of the relative rate ratio of N-chloro-N-methylacetamide (N-Me @ 5.7δ) to N-chloro-N-t-butylacetamide (acyl-Me @ 3.9δ). Dioxane was internal standard at 6.7δ . The other significant peaks recorded in these spectra are side bands.

use of a planimeter.

Preparation of the ampoules of the amide with benzoyl peroxide was identical to that for the amides with PAT. The benzoyl peroxide ampoules were wrapped in aluminum foil and refluxed in a boiling water bath for five hours.

Photolysis was accomplished by use of a General Electric 275 w, 110-125 v sunlamp at 2-ft distance from nmr tubes containing the solution. In one part of the photolysis study the irradiation was done in the esr cavity with a 2,000 watt PEK AH6-2B high pressure mercury lamp at 0° and $-90^{\circ}C$.

C. Syntheses

The N-chloramides were all prepared by a reaction of the parent amide with tert-butylhypochlorite in carbon tetrachloride solvent with a small amount of potassium carbonate added.[9] The mixture was allowed to stir at room temperature for a period of time from several hours to several days depending on the particular amide. In some instances there was necessity to reflux the mixture. In a few cases where chlorination occurred only slowly, a few drops of bromine were added with the tert-butylhypochlorite being the solvent as well as the reactant. The completion of the reaction was determined by nmr. There was a downfield shift of 0.2 to 0.3 ppm of the protons in the methyl group adjacent to the carbonyl group in the chlorinated amide. The solvent and low boiling materials were removed by the roto-vap and the N-chloramide was collected by vacuum distillation.

The tert-butylhypochlorite was synthesized[44] by adding a mixture of tert-butanol and glacial acetic acid to a solution of common house-

hold bleach at ice bath temperature and allowed to stir for a few minutes. The yellow oily layer was then separated and washed with sodium carbonate and water to remove any acid and dried over calcium chloride. It was stored in an amber bottle under refrigeration at ca. 0°C.

N-chloro-N-tert-butylacetamide: The N-tert-butylacetamide used in this preparation was synthesized in 56% yield from acetyl chloride and tert-butylamine by a procedure similar to that of Schlatter,[45] mp 96-97°C (lit.[46] 98°). NMR (CCl_4) δ 1.30 (s, 9H, $C(CH_3)_3$) 1.85 (s, 3H, CH_3); ir (CCl_4) 3280 (N-H) and 1650 cm^{-1} (C=O). The N-chloramide was synthesized in 33% yield from 6.9 g (0.060 mol) N-tert-butylacetamide and 7.2 g (0.067 mol) tert-butylhypochlorite, bp 30° (4.4 mm) [lit.[9] 44° (9 mm)]. NMR (CCl_4) δ 1.45 (s, 9H, $C(CH_3)_3$) 2.15 (s, 3H, CH_3); ir (CCl_4) 1680 cm^{-1} (C=O).

N-chloro-N-methylacetamide: This compound was synthesized in 51% yield from 4.88 g (0.067 mol) N-methylacetamide and 7.77 g (0.072 mol) tert-butylhypochlorite, bp 35-37° (17 mm) [lit.[9] 42° (24 mm)]. NMR (CCl_4) δ 2.15 (s, 3H, CH_3) 3.25 (s, 3H, CH_3).

N-chloro-N-ethylacetamide: The synthesis of N-chloro-N-ethylacetamide was achieved in 62% yield from 6.13 g (0.070 mol) N-ethylacetamide, 8.09 g (0.074 mol) tert-butylhypochlorite and 2 drops bromine, bp 29-30° (7.4 mm). NMR (CCl_4) δ 1.20 (t, 3H, J = 7.0 Hz, CH_3) 2.15 (s, 3H, CH_3) 3.70 (q, 2H, J = 7.0 Hz, CH_2).

N-chloro-N-n-propylacetamide: The N-n-propylacetamide used in this preparation was synthesized in 42% yield from n-propylamine and acetyl chloride. Acetyl chloride diluted with dry benzene was added dropwise to the amine in benzene solvent at ice bath temperature containing a 3-fold excess of triethylamine. Following the last addition the mix-

ture was allowed to warm to room temperature and to stir for ca. 3 h. N-n-propylacetamide was collected via vacuum distillation of the filtrate from the reaction mixture, bp 98° (6.5 mm). NMR (CCl_4) δ 0.90 (t, 3H, J = 6.0 Hz, CH_3) 1.50 (s, 2H, J = 6.0 Hz, CH_2) 1.90 (s, 3H, CH_3) 3.10 (q, 2H, J = 6.0 Hz, CH_2) 7.50 (b s, 1H, NH). Reaction of 5.21 g (0.052 mol) N-n-propylacetamide and 7.70 g (0.071 mol) tert-butylhypochlorite produced N-chloro-N-n-propylacetamide in 37% yield, bp 44° (6.8 mm). NMR (CCl_4) δ 0.90 (t, 3H, J = 7.0 Hz, CH_3) 1.70 (s, 2H, J = 7.0 Hz, CH_2) 2.15 (s, 3H, CH_3) 3.60 (t, 2H, J = 7.0 Hz, CH_2).

N-chloro-N-isopropylacetamide: The N-isopropylacetamide used in this preparation was synthesized in 75% yield from isopropylamine and acetyl chloride by the same method as N-n-propylacetamide, bp 41-42° (0.1 mm). NMR (CCl_4) δ 1.10 (d, 6H, J = 6.0 Hz, $C(CH_3)_2$) 1.85 (s, 3H, CH_3) 3.95 (o, 1H, J = 6.0 Hz, CH) 7.60 (b s, 1H, NH); ir (CCl_4) 3230 (N-H) and 1650 cm^{-1} (C=O). N-chloro-N-isopropylacetamide was produced in 64% yield from 8.9 g (0.088 mol)N-isopropylacetamide and 9.12 g (0.084 mol) tert-butylhypochlorite, bp 27-29° (3.8 mm). NMR (CCl_4) δ 1.15 (d, 6H, J = 6.0 Hz, $C(CH_3)_2$) 2.15 (s, 3H, CH_3) 4.85 (s, 1H, J = 6.0 Hz, CH); ir (CCl_4) 1670 cm^{-1} (C=O).

N-chloro-N-phenethylacetamide: N-Phenethylacetamide used in this synthesis was produced in 43% yield from phenethylamine and acetyl chloride by the same manner as N-n-propylacetamide, bp 140-143° (1.8 mm) [lit.[47] 143-146° (1 mm)], mp 48-50° (lit.[47] 53.5-54°). NMR (CCl_4) δ 1.90 (s, 3H, CH_3) 2.70 (t, 2H, J = 7.0 Hz, CH_2) 3.30 (q, 2H, J = 7.0 Hz, CH_2) 7.10 (s, 5H, C_6H_5) 7.75 (b s, 1H, NH); ir (CCl_4) 3230 (N-H) and 1650 cm^{-1} (C=O). Reaction of 6.87 g (0.042 mol) N-phenethylacetamide and 8.00 g (0.074 mol) tert-butylhypochlorite produced N-chloro-N-phenethylacet-

amide in 68% yield, bp 92-96° (0.6 mm). NMR (CCl_4) δ 2.10 (s, 3H, CH_3) 2.90 (t, 2H, J = 7.0 Hz, CH_2) 3.85 (t, 2H, J = 7.0 Hz, CH_2) 7.15 (s, 5H, C_6H_5); ir (CCl_4) 1670 cm^{-1} (C=O).

N-chloro-N-neopentylacetamide: The N-neopentylacetamide used in the synthesis of this N-chloramide was produced from neopentyl amine and acetyl chloride by the same method as for N-n-propylacetamide in 85% yield, bp 113-116° (10 mm) [lit.[47] 114-115° (10 mm)], mp 55° (lit.[47] 65-66°). NMR (CCl_4) δ 0.85 (s, 9H, $(CH_3)_3C$) 1.90 (s, 3H, CH_3) 2.95 (d, 2H, J = 6.0 Hz, CH_2) 7.60 (b s, 1H, NH); ir (CCl_4) 3280 (N-H) and 1650 cm^{-1} (C=O). N-chloro-N-neopentylacetamide was synthesized from 5.17 g (0.040 mol) N-neopentylacetamide and 5.27 g (0.048 mol) tert-butylhypochlorite, bp 67-68° (5 mm). NMR (CCl_4) δ 0.95 (s, 9H, $(CH_3)_3C$) 2.20 (s, 3H, CH_3) 3.50 (s, 2H, CH_2); ir (CCl_4) 1680 cm^{-1} (C=O).

N-chloro-N-(1,1-dimethyl-2-phenethyl)acetamide: N-(1,1-Dimethyl-2-phenethyl)acetamide was synthesized from acetyl chloride and 1,1-dimethyl-2-phenethylamine in 40% yield according to the same procedure as used in the preparation of N-n-propylacetamide, mp 92°. NMR (CCl_4) δ1.25 (s, 6H, $(CH_3)_2$) 1.75 (s, 3H, CH_3) 2.95 (s, 2H, CH_2) 7.10 (s, 5H, C_6H_5); ir (CCl_4) 3280 (N-H) and 1670 cm^{-1} (C=O). N-chloro-N-(1,1-dimethyl-2-phenethyl)acetamide was synthesized from 5.26 g (0.028 mol) N-(1,1-dimethyl-2-phenethyl)acetamide and 3.28 g (0.030 mol) tert-butyhypochlorite in 36% yield, bp 80-83° (0.4 mm). NMR (CCl_4) δ 1.45 (s, 6H, $(CH_3)_2C$) 2.15 (s, 3H, CH_3) 3.10 (s, 2H, CH_2) 7.10 (s, 5H, C_6H_5); ir (CCl_4) 1680 cm^{-1} (C=O).

N-chloro-N-α,α-dimethylbenzylacetamide: N-α,α-Dimethylbenzylacetamide was synthesized from α-methylstyrene and acetonitrile according to the procedure of Ritter and Minieri,[48] mp 95-97° (lit.[48] 96-97°), bp 97-105°

(0.25 mm). NMR (CCl_4) δ 1.40 (s, 6H, $(CH_3)_2C$) 1.55 (s, 3H, CH_3) 7.10 (s, 5H, C_6H_5) 7.45 (b s, 1H, NH); ir (CCl_4)3280 (N-H) and 1670 cm^{-1} (C=O). N-chloro-N-α,α-dimethylbenzylacetamide was synthesized from 2.26 g (0.013 mol) N-α,α-dimethylbenzylacetamide and 1.90 g (0.018 mol) tert-butylhypochlorite in 64% yield, bp 27° (0.3 mm). NMR (CCl_4) δ 1.75 (s, 6H, $(CH_3)_2C$) 2.15 (s, 3H, CH_3) 7.20 (s, 5H, C_6H_5) ; ir (CCl_4) 1680 cm^{-1} (C=O).

N-chloro-N-(1-methyl-1-benzylmethylacetate)acetamide: A hydantion was first prepared in this synthesis in 74% yield from phenyl acetone and sodium cyanide in a mixture of ammonium carbonate and 60% ethanol.[49] Hydrolysis[50] of this hydantion produced α-methylphenylalanine in 71% yield. Esterification[51] gave the desired amine in 72% yield. The amine was then used to produce N-(1-methyl-1-benzylmethylacetate) acetamide according to the same procedure as for N-n-propylacetamide, mp 116-118°. NMR (CCl_4) δ 1.60 (s, 3H, CH_3) 1.85 (s, 3H, CH_3) 3.10 (s, 1H, CH_2) 3.45 (s, 1H, CH_2) 3.70 (s, 3H, CH_3) 7.10 (m, 5H, C_6H_5); ir (CCl_4) 3330 (N-H) 1740 (C=O) and 1680 cm^{-1} (C=O). Reaction of 3.61 g (0.015 mol) N-(1-methyl-1-benzylmethylacetate)acetamide and 2.35 g (0.022 mol) tert-butylhypochlorite produced the N-chloramide in 70% yield, bp 113° (0.05-0.1 mm). NMR (CCl_4) δ 1.40 (s, 3H, CH_3) 2.20 (s, 3H, CH_3) 3.05 (s, 1H, CH_2) 3.35 (s, 1H, CH_2) 3.60 (s, 3H, CH_3) 7.10 (m, 5H, C_6H_5).

N-chloro-N-(tert-butyl)phenylacetamide: The phenylacetyl chloride used in this synthesis was prepared from phenylacetic acid and thionyl chloride in 70% yield.[52] N-(tert-Butyl)phenylacetamide was synthesized in 36% yield from phenylacetyl chloride and tert-butylamine in a procedure similar to that for N-n-propylacetamide, bp 140-150° (0.2 mm).

NMR (CCl_4) δ 1.25 (s, 9H, $(CH_3)_3C$) 3.35 (s, 2H, CH_2)3.60 (s, 1H, NH) 7.20 (s, 5H, C_6H_5). Reaction of 4.96 g (0.026 mol) N-(tert-butyl) phenylacetamide and 4.53 g (0.042 mol) tert-butylhypochlorite produced N-chloro-N-(tert-butyl)phenylacetamide in 56% yield, bp 88° (0.2 mm). NMR (CCl_4) δ 1.40 (s, 9H, $(CH_3)_3C$) 3.75 (s, 2H, CH_2) 7.15 (s, 5H, C_6H_5); ir (CCl_4) 1680 cm^{-1} (C=O).

N-chloro-N-tert-butylbenzamide: N-tert-Butylbenzamide was synthesized from benzoyl chloride and tert-butylamine as in the procedure described for N-n-propylacetamide, mp 120-125° (lit.[46] 135°). NMR (CCl_4) δ 1.40 (s, 9H, $(CH_3)_3C$) 7.40 (m, 5H, C_6H_5). Reaction of 10.8 g (0.061 mol) N-tert-butylbenzamide and 18.1 g (0.17 mol) tert-butylhypochlorite produced N-chloro-N-tert-butylbenzamide, bp 76-78° (0.2 mm). NMR (CCl_4) δ 1.55 (s, 9H, $(CH_3)_3C$) 7.40 (m, 5H, C_6H_5); ir (CCl_4) 1680 cm^{-1} (C=O).

N-chloro-N-cyclopropylacetamide: The N-cyclopropylacetamide used in this synthesis was prepared from N-cyclopropylamine and acetyl chloride according to Paquette, et al.,[53] in 34% yield, bp 67-68° (0.2 mm). NMR (CCl_4) δ 0.65 (d, 4H, J = 8.0 Hz, CH_2CH_2) 1.90 (s, 3H, CH_3) 2.70 (m, 1H, CH) 7.60 (b s, 1H, NH); ir (CCl_4) 3230 (N-H) and 1650 cm^{-1} (C=O). N-chloro-N-cyclopropylacetamide was synthesized in 92% yield from 2.98 g (0.030 mol) N-cyclopropylacetamide and 15 ml tert-butylhypochlorite with two drops Br_2, bp 58-59° (4.3 mm). NMR (CCl_4) δ 0.95 (d, 4H, J = 4.0 Hz, CH_2CH_2) 2.20 (s, 3H, CH_3) 2.95 (m, 1H, J = 4.0 Hz, CH); ir (CCl_4) 1710 cm^{-1} (C=O).

N-chloro-2-pyrrolidone: Reaction of 5.13 g (0.060 mol) 2-pyrrolidone and 7.65 g (0.070 mol) tert-butylhypochlorite produced N-chloro-2-pyrrolidone in 86% yield, mp 51-52°. NMR (CCl_4) δ 1.20 (m, 2H, CH_2)

1.80 (t, 2H, J = 6.0 Hz, CH_2) 2.80 (t, 2H, J = 6.0 Hz, CH_2).

N-chloro-2-piperidone: Cyclopentanone oxime was prepared in 56% yield from cyclopentanone and hydroxylamine sulfate according to Fox, et al.,[54] bp 57-61° (0.3-0.5 mm) [lit.[54] 93-97° (24 mm)]. The 2-piperidone was synthesized[55] in 26% yield by treatment of cyclopentanone oxime with sulfuric acid, bp 71-73° (0.2 mm) [lit.[55] 105-110° (2-4 mm)]. NMR (CCl_4) δ 1.75 (m, 4H, CH_2CH_2) 2.20 (m, 2H, CH_2) 3.30 (m, 2H, CH_2); ir (CCl_4) 3175 (N-H) and 1670 cm^{-1} (C=O). Reaction of 2.87 g (0.029 mol) 2-piperidone and 3.84 g (0.035 mol) tert-butylhypochlorite produced N-chloro-2-piperidone in 65% yield, bp 61-62° (0.1 mm). NMR (CCl_4) δ 1.95 (m, 4H, CH_2CH_2) 2.50 (t, 2H, J = 6.0 Hz, CH_2) 3.75 (t, 2H, J = 6.0 Hz, CH_2).

N-chloro-2,2,6,6-tetramethylpiperidine: Reaction of 6.36 g (0.045 mol) 2,2,6,6-tetramethylpiperidine and 8.92 g (0.067 mol) N-chlorosuccinimide in anhydrous ether produced N-chloro-2,2,6,6-tetramethylpiperidine in 45% yield, bp 36° (0.65 mm). NMR (CCl_4) δ 1.20 (s, 12H, $(CH_3)_2C$, $(CH_3)_2C$) 1.60 (s, 6H, $CH_2CH_2CH_2$).

IX. References

(1) Y. L. Chow and A. C. H. Lee, Chem. and Ind., 827 (1967).

(2) Y. L. Chow, J. N. S. Tam and A. C. H. Lee, Can. J. Chem., 47, 2441 (1969).

(3) L. P. Kuhn, G. G. Kleinspehn and A. C. Duckworth, J. Am. Chem. Soc., 89, 3858 (1967).

(4) J. N. S. Tam, R. W. Yip and Y. L. Chow, ibid., 96, 4543 (1974).

(5) R. S. Neale, Synthesis, 1 (1971).

(6) O. E. Edwards and J. N. Paton, Can. J. Chem., 49, 1648 (1971).

(7) M. E. Kuehne and D. A. Horne, J. Org. Chem., 40, 1287 (1975).

(8) A. L. J. Beckworth and J. E. Goodrich, Aust. J. Chem., 18, 747 (1965).

(9) R. S. Neale, N. L. Marcus and R. G. Schepers, J. Am. Chem. Soc., 88, 3051 (1966).

(10) T. Koenig, J. A. Hoobler, C. E. Klopfenstein, G. Hedden, F. Sunderman and B. R. Russell, ibid., 96, 4573 (1974).

(11) W. C. Danen and R. W. Gellert, ibid., 94, 6853 (1972).

(12) C. Brown and A. J. Lawson, Tetrahedron Lett., 191 (1975).

(13) W. C. Danen and F. A. Neugebauer, Angew. Chem. Int. Ed. Engl., 14, 783 (1975).

(14) R. W. Gellert, M. S. Thesis, Kansas State University, (1973).

(15) C. T. West, Ph. D. Thesis, Kansas State University, (1972).

(16) W. C. Danen, in "Methods in Free-Radical Chemistry", Vol. 5, E. S. Huyser, Ed., Marcel Dekker, Inc., New York, 1974, Chapter 1.

(17) E. Hayon, T. Ibata, N. N. Lichtin and M. Simic, J. Am. Chem. Soc., 93, 5388 (1971).

(18) P. D. Bartlett and R. R. Hiatt, ibid., 80, 1398 (1958).

(19) D. Griller and K. U. Ingold, Accts. Chem. Res., 9, 13 (1976).

(20) J. F. Bunnett, in "Investigation of Rates and Mechanisms of Reactions, Part I", E. S. Lewis, Ed., Wiley-Interscience, New York, 1974, Chapter IV.

(21) E. J. Walsh and H. C. Kuivila, J. Am. Chem. Soc., 88, 576 (1966).

(22) E. L. Bauer, "A Statistical Manual for Chemists", 2nd ed., Academic Press, New York, 1971, pp. 17, 23.

(23) R. A. Johnson and F. D. Greene, J. Org. Chem., 40, 2186 (1975).

(24) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions", John Wiley & Sons Inc., New York, 1963, pp. 223, 229.

(25) S. W. Benson, J. Chem. Ed., 42, 502 (1965).

(26) W. C. Danen and R. L. Winter, J. Am. Chem. Soc., 93, 716 (1971).

(27) W. C. Danen, D. G. Saunders and K. A. Rose, ibid., 95, 1612 (1973).

(28) S. F. Nelsen and R. T. Landis II, ibid., 95, 8707 (1973).

(29) J. Cantacuzene, J. Leroy, R. Jantzen and F. Dudragne, ibid., 94, 7924 (1972).

(30) C. N. R. Rao, K. G. Rao, A. Goel and D. Balasubramanian, J. Chem. Soc. (A), 3077 (1971).

(31) A. S. N. Murthy, K. G. Rao and C. N. R. Rao, J. Am. Chem. Soc., 92, 3544 (1970).

(32) B. M. Rode and R. Fussenegger, J. Chem. Soc. Faraday Trans. II, 71, 1958 (1976).

(33) W. E. Stewart and T. H. Siddall, Chem. Rev., 70, 517 (1970).

(34) R. M. Hammaker and B. A. Gugler, J. Mol. Spectr., 17, 356 (1965).

(35) L. Isbrandt, W. C-T. Tung, and M. T. Rogers, J. Magn. Resonance, 9, 461 (1973).

(36) J. F. Yan, F. A. Momany, R. Hoffman and H. A. Scheraga, J. Phys. Chem., 74, 420 (1970).

(37) L. Srinivasa Rao, V. V. Chalapathi and K. V. Ramiah, Proc. Indian Acad. Sci., 81, 256 (1975).

(38) M. F. Robin, F. A. Bovey and H. Basch in "The Chemistry of Amides", J. Zabicky, Ed., Interscience, New York, 1970, Chapter 1.

(39) R. F. Bridger and G. A. Russell, J. Am. Chem. Soc., 85, 3754 (1963).

(40) Y. L. Chow and J. N. S. Tam, J. Chem. Soc. (C), 1138 (1970).

(41) C. Walling and R. T. Clark, J. Am. Chem. Soc., 96, 4530 (1974).

(42) J. R. Roberts and K. U. Ingold, ibid., 95, 3228 (1973).

(43) E. E. J. Dekker, J. B. F. N. Engberts and T. J. deBoer, Tetrahedron Lett., 2651 (1969).

(44) M. J. Hintz and C. Walling, Organic Syntheses, 49, 9 (1969).

(45) M. J. Schlatter, J. Am. Chem. Soc., 63, 1735 (1941).

(46) R. B. Wagner and H. D. Zook, "Synthetic Organic Chemistry", John Wiley & Sons, Inc., New York, 1953, p. 578.

(47) M. E. Smith and H. Adkins, J. Am. Chem. Soc., 60, 657 (1938).

(48) J. J. Ritter and P. P. Minieri, ibid., 70, 4048 (1948).

(49) L. H. Goodson, I. L. Honigberg, J. J. Lehman and W. H. Burton, J. Org. Chem., 25, 1922 (1960).

(50) R. M. Herbst and T. B. Johnson, J. Am. Chem. Soc., 54, 2463 (1932).

(51) B. F. Erlanger, H. Sachs and E. Brand, ibid., 76, 1806 (1954).

(52) L. Fieser and M. Fieser, "Reagents for Organic Synthesis", 1, John Wiley & Sons, New York, 1967, p. 1159.

(53) L. A. Paquette, J. R. Malpass and G. R. Krow, J. Am. Chem. Soc., 92, 1989 (1970).

(54) S. W. Fox, M. S. Dunn and M. P. Stodard, J. Org. Chem., 6, 411 (1941).

(55) A. Chatterjee and C. P. Dutta, Tetrahedron, 23, 1779 (1967).

X. Acknowledgements

I wish to thank Dr. Danen, my advisor for his untiring assistance and guidance throughout this research project. I would like to express my appreciation to the faculty and graduate students for their many helpful suggestions. A special note of thanks to Dr. Paukstelis who has given much assistance regarding use of the nmr and in the interpretation of data.

Appreciation is also expressed to Marymount College for providing the opportunity and financial support for this education.

XI. Vita

Sister Mary Therese Blecha was born in Belleville, Kansas on April 15, 1941. She graduated from Belleville High School in 1959. She then attended Marymount College until 1962 at which time she entered the Congregation of the Sisters of St. Joseph at Concordia, Kansas. In 1965 she was awarded the Bachelor of Science degree in chemistry by Marymount College.

Following the attainment of this degree she taught chemistry and biology classes in high school for seven years and also taught freshman chemistry for one year at Marymount College. During part of her teaching career she was enrolled in a graduate science education program at the University of North Dakota and was awarded the Master Science Teaching degree by this University in 1971.

In 1973 she entered the Graduate School at Kansas State University to work on a Master's degree in chemistry.

RELATIVE RATES OF ABSTRACTION OF CHLORINE BY PHENYL RADICALS FROM N-CHLORAMIDES

by

SISTER MARY THERESE BLECHA

B. S., Marymount College, 1965
M. S. T., University of North Dakota, 1971

AN ABSTRACT OF A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1976

ABSTRACT

There has been much investigation of reactions involving the N-halamides and in particular photolytic rearrangements of the amido radical and formation of new compounds. In these studies the main emphasis has been on the usefulness of these reactions in organic syntheses rather than on the amido radical itself. It was therefore, the purpose of this study to determine the relative rates of chlorine abstraction from various N-chloro-N-substituted amides and to probe the facility with which amido radicals undergo decomposition via a unimolecular β-elimination reaction.

The chlorine was abstracted by phenyl radicals which were formed from the thermal decomposition of phenylazotriphenylmethane. The N-chloramides, RCONClR' were varied from a simple R' group as R' = Me to R' groups of considerable size and bulkiness as R' = $C(CH_3)(COOCH_3)$-CH_2Ph. Though the differences in the rates of chlorine abstraction were small, there was evidence of a definite trend being dependent on the size and bulkiness of the R and/or R' groups. From the results of the kinetic studies it was concluded that the relative rate of chlorine abstraction from the N-chloramides was most likely dependent on steric effects. The steric effects could cause a lowering of the rotational barrier height and thus allow for a more facile phenyl radical attack. They also could be the source of an added driving force for the reaction by causing internal strain which would be relieved during the reaction.

The rate of abstraction from N-chloro-N-methylacetamide did not fit into this trend and was faster than anticipated when considering the other N-chloramides. No completely satisfying explanation for

this anomaly was found although the explanation may lie in the fact of the compound having a uniquely different conformation.

A study of the reaction products resulting from the chlorine abstraction reactions via the phenyl radical gave no indication of any β-elimination products. Hence, it was concluded that under the conditions of these reactions β-elimination did not occur to any signifcant extent.

Several of the N-chloramides were submitted separately to photolysis reactions for the purpose of further study of subsequent amido radical reactions. The major reaction occurring was that of formation of the parent amide presumably via chlorine atom-HCl chain. In the presence of a chlorine atom trap the parent amide was again formed but this time probably via hydrogen abstraction from the solvent.

The determination of the rate of chlorine abstraction from an N-chloramine, N-chloro-2,2,6,6-tetramethylpiperidine, was also included in this study to allow for a comparison of the rate of chlorine abstraction from an amide to that from an amine. The rate for the amine was comparable to that for the amides.