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# Polar Radicals XVIII.[1] On the Mechanism of Chlorination By N-Chloroamines: Intermolecular and Intramolecular Abstraction.

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## ABSTRACT

The photochlorinations of the n-butyl, n-pentyl, and n-hexyltrimethylammonium chlorides, using molecular chlorine in hexachloroacetone or 15% $CD_3CO_2D$/85% $H_2SO_4$, or using N-chlorodimethylamine in the acid solvent are described. The ammonium group exerted a strong polar directing effect upon the site of substitution. This effect was found to be more pronounced in the more polar protic solvent. The reagent, N-chlorodimethylamine, generated the dimethylamminium radical, whose reaction showed a polar sensitivity toward hydrogen abstraction similar to that of the chlorine atom, but exhibiting a much greater secondary/primary selectivity. Comparison of the isomer distributions obtained from the self photochlorination reactions of N-chloro-n-hexylmethylamine and N-chloro-n-pentylmethylamine in the acid solvent, with the distribution pattern obtained for the chlorinations of the ammonium salts with N-chlorodimethylamine, suggested that the self chlorinations of the N-chloroamines proceed by the intramolecular hydrogen abstraction mechanism suggested previously.

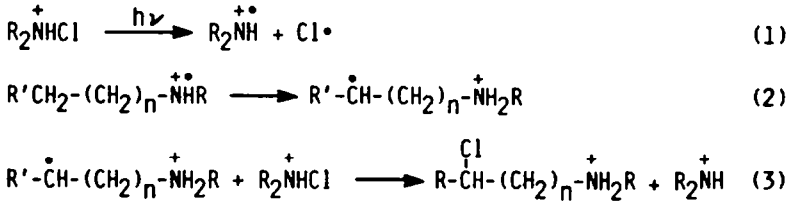
## INTRODUCTION

The acid-catalyzed chlorination reactions of N-chloroamines can be conveniently divided into two mechanistic classifications; those involving intramolecular hydrogen abstraction and those proceeding by bimolecular hydrogen atom transfer. The intramolecular chlorinations, known as the Hofmann-Löffler-Freytag (HLF) reaction,[3] have been used extensively in the synthesis of a variety of nitrogen containing hetrocyclic compounds, and is the classic method for the synthesis of pyrrolidines.[3-18] In the intramolecular reactions the N-chloroamine undergoes initiated self chlorination and the product mixture is usually treated with base, without isolating the intermediate halide. Intramolecular cyclization yields five or six membered ring heterocyclic products arising from nucleophilic substitution of the halogen by the free amine. The intermolecular reactions have used N-chloroamines as reagents to produce a variety of selectively halogenated compounds which do not contain an amine functional group.

The first examples of the intramolecular reaction were reported by Hofmann[11,19] and the utility of the reaction was later extended by Löffler and Freytag.[20-22] The results of numerous other studies are well documented in a review by Wolff.[3] The first study of the mechanism of the reaction was reported

[1] For part XVII of this series, see: Ref. 1.

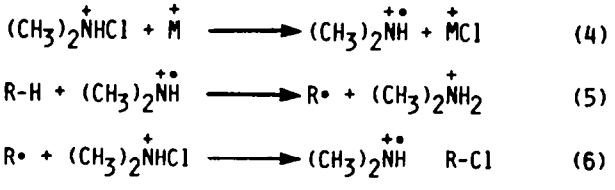
by Wawzonek, Thelan and Nelson.[7] The free radical chain mechanism proposed for the reaction is given in Scheme I.



**Scheme I**

Corey and Hertler confirmed the mechanistic conclusions of Wawzonek and extended the understanding of the mechanism in their subsequent study.[5]

In the course of an investigation of the amination of a variety of substituted benzenes using N-chloroamines Minisci, Galli and Cecere[24] reported that benzyl chlorides were produced as side products when the reactions contained substituted toluenes. They initiated a series of investigations of the intermolecular chlorination and bromination of various substituted alkanes using N-haloamines and a variety of initiators.[25-27] The reagents showed very high selectivities and the reactions using N-chloroamines gave similar selectivities to those using N-bromoamines. They also found that the selectivity observed was dependent upon the initiator used, with cuprous salts giving the highest selectivity and ferrous salts giving the lowest selectivity. On the basis of these results, but contrary to the suggested change in selectivity with changing initiator, they proposed the following mechanism (Scheme II):



**Scheme II**

Minisci reported a high selectivity for hydrogen abstraction at the second carbon of heptane.[27] He proposed that this high selectivity was caused by the steric bulkiness of the dialkylamminium radical, and that the second carbon has the least hindered secondary hydrogen.

Tanner and Mosher[28] reported that intermolecular hydrogen abstractions, from substituted alkanes carried out using metal ion initiated N-chloroamines, which had been synthesized by the procedure of Coleman[2] (the synthetic method), did not proceed via an amminium radical, but rather via a chlorine atom chain (see Scheme III).

$$RH + Cl^{\bullet} \longrightarrow R^{\bullet} + HCl \qquad (7)$$

$$HCl + R_2^{+}NHCl \longrightarrow Cl_2 + R_2^{+}NH_2 \qquad (8)$$

$$R^{\bullet} + Cl_2 \longrightarrow RCl + Cl^{\bullet} \qquad (9)$$

**Scheme III**

The isomer distributions found were rationalized as being controlled by polar effects which deactivated the C-H bonds closest to the electronegative group. It was also reported that, for several substrates previously studied, the differences in selectivities observed were also due to the instability of the products of chlorination in the acidic solvent (85% $H_2SO_4$/15% $CH_3CO_2H$). Although product instability was contested by Minisci[29] and by Deno[30] the effect of solvolysis on the product ratios was subsequently confirmed by Deno.[31]

The apparent discrepancy in the results obtained by the two groups (Minisci and Tanner) was clarified by Spanswick and Ingold.[32] They found that the important factor was the purity of the N-chloroamine. The N-chloroamines investigated were purified using Minisci's method[33] by precipitation from ether as their hydrosulphate salts. The crystalline salt was washed with ether, dried and dissolved in the solvent of choice and stored in the absence of light at -78°C until it was used. Reactions of N-chlorodimethylamine and N-chloropiperidine, purified in this manner, with 1-chlorobutane in 4M $H_2SO_4/CH_3CO_2H$ gave isomer distributions clearly different from those obtained with molecular chlorine. Various initiators were used and found to give varying results. Ferrous sulphate, cerous sulphate, cerous chloride and cobaltous chloride all gave results which were closer to those obtained using molecular chlorine. The incursion of a chlorine atom chain was proposed to be the cause behind the variation in values obtained by Minisci.[25] On the basis of their studies Spanwick and Ingold[32] concluded that careful purification of the N-haloamine is necessary in order to observe the reactivity of an amminium radical chain. The synthetic method was not considered to produce N-haloamines of sufficient purity to eliminate the participation of a chlorine atom chain.

Deno reported the results obtained from the chlorination of a number of aliphatic alcohols, ethers, carboxylic acids and amides with N-chlorodiisopropylamine in strong acid.[30] The reactions of the chloroamines, unlike those carried out with molecular chlorine, gave primarily (ω-1) chlorination. The quantitative conclusions reached from these studies, however, were subsequently retracted since the product mixtures were unstable, and underwent differential hydrolysis in the acid media.[31] The authors concluded, nevertheless, that (ω-1) halogenation was still the dominant reaction.

Using N-chlorodiisopropylamine Deno and Jedziniak[34] chlorinated lauramide using 80% $H_2SO_4$/20% $H_2O$ and palmitamide in 30% $H_2SO_4$/70% $CH_3CO_2H$. Since 88% of the chlorination occurred on C8-C10 for both amides, a novel explanation was invoked. Because of the hydrophobic nature of the long aliphatic chains, Deno proposed that the carbon skeleton folds back on itself to minimize exposure to the solvent. When this occurred, the positions furthest removed from the polar amido group are C8-C10 and are thus the favored sites for hydrogen abstraction by the diisopropylamminium radical.

The chain propagation sequence for the intermolecular halogenation reactions, where product stability is not a consideration, appear to be reasonably

well understood. It was suggested that, on the basis of the selective production of pyrrolidine products, the mechanism of the halogenations of long chain aliphatic N-chloroamine proceeded by an intramolecular abstraction by a nitrogen-centered radical. It was not shown, however, that this mechanism could be distinguished from an intermolecular abstraction by either a chlorine atom, or a nitrogen-centered radical which showed similar selectivities. In light of the conclusions of Tanner and Mosher,[28] and Ingold and Spanswick[32] it appeared to be an important question to address.

## RESULTS

Since the amine and N-chloroamine substrates are considered to be almost completely protonated in the strong acid, the substrates n-butyltrimethylammonium chloride (**1**), n-pentyltrimethylammonium chloride (**2**), and n-hexyltrimethylammonium chloride (**3**) were chlorinated using molecular chlorine or N-chlorodimethylamine to investigate the polar effects exerted by the positive charge. N-Chlorodimethylamine was chosen as a source of a representative amminium radical, since it had been shown to give selectivities differing from the chlorine atom.[32] A mixed acid, 15% $CD_3CO_2D$/85% $H_2SO_4$, was chosen as being representative of the solvents normally employed for the reaction. To measure the influence of the solvent upon the selectivity of the chlorine atom, a less polar aprotic solvent, hexachloroacetone, was also used with molecular chlorine. To investigate the possible importance of unprotonated amine as the substrate, since it is always in equilibrium with the protonated amine, n-pentyldimethylamine (**4**) was also subjected to the chlorinations. Finally as models for the investigation of a potential intramolecular abstraction process, the reactions of N-chloro-N-methyl-n-pentylamine (**5**) and N-chloro-N-methyl-n-hexylamine (**6**) in 15% $CD_3CO_2D$/85% $H_2SO_4$ were studied.

The Photochlorination of the Quaternary Ammonium Salts in Hexachloroacetone - Substrates **1**, **2**, and **3** were photochlorinated with molecular chlorine in hexachloroacetone at 30°C. Qualitatively these chlorinations were quite slow, taking more than 6 hours to complete. The chlorination of 1-chlorobutane, for example, when run under similar conditions was complete in about 1 hour. The product yields were determined by NMR analysis.

The reactivities of each hydrogen relative to the primary hydrogens of the longest alyphatic chain in each of the quaternary salts are given in Table I.

The Photochlorination of the Quaternary Ammonium Salts in 15% $CD_3CO_2D$/85% $H_2SO_4$ - Substrates **1**, **2**, and **3** were photochlorinated with molecular chlorine in 15% $CD_3CO_2D$/85% $H_2SO_4$ at 30°C. Qualitatively, these chlorinations required similar reaction times to those run using hexachloroacetone as the solvent. The product mixtures were analyzed by NMR. The reactivities of the various hydrogens are given in Table II.

The Reaction of the Quaternary Ammonium Salts with N-Chlorodimethylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$ - The quaternary ammonium salts **1**, **2**, and **3** were photochlorinated with N-chlorodimethylamine at 30°C in 15% $CD_3CO_2D$/85% $H_2SO_4$. The reactions were qualitatively quite slow, taking up to 120 hours for complete reaction of the N-chloroamine. The reaction with the n-hexyl salt, **3**, however,

Table I. Relative Reactivities/H in the Chlorinations of n-Butyltrimethylammonium Chloride, n-Pentyltrimethylammonium Chloride, and n-Hexyltrimethylammonium Chloride with Molecular Chlorine in Hexachloroacetone.[a]

| Reaction # | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ | | |
|---|---|---|---|---|---|---|---|
| 1 | 0.0[b] (0)[d] | 0.0 (0) | 0.07±0.09[c] (1.5) | 3.0±0.6 (66) | 1.0 (33) | | |
| | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ | |
| 2 | 0.0 (0) | 0.0 (0) | 0.0 (0) | 1.8±0.6 (24) | 4.1±1.1 (55) | 1.0 (20) | |
| | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ |
| 3 | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 2.3±0.7 (28) | 4.4±1.4 (54) | 1.0 (18) |

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.05.
c. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
d. (Percent yield), based on total products formed.

Table II. Relative Reactivities/H in the Chlorinations of n-Butyltrimethylammonium Chloride, n-Pentyltrimethylammonium Chloride, and n-Hexyltrimethylammonium Chloride with Molecular Chlorine in 15% $CD_3CO_2D$/85% $H_2SO_4$.[a]

| Reaction # | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ | | |
|---|---|---|---|---|---|---|---|
| 4 | 0.0[b] (0)[d] | 0.0 (0) | 0.0 (0) | 2.1±0.4[c] (58) | 1.0 (42) | | |
| | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ | |
| 5 | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.77±0.16 (21) | 1.4±0.2 (38) | 1.0 (41) | |
| | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ |
| 6 | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.73±0.08 (21) | 1.2±0.2 (35) | 1.0 (44) |

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
c. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
d. (Percent yield), based on total products formed.

was complete in 24 hours, as was its reaction with molecular chlorine. The product mixtures were analyzed by NMR and the results are listed in Table III.

The Chlorinations of n-Pentyldimethylamine (4) in 15% $CD_3CO_2D$/85% $H_2SO_4$ - The chlorinations of amine 4 in 15% $CD_3CO_2D$/85% $H_2SO_4$ with molecular chlorine, and with N-chlorodimethylamine were carried out in order to determine the reactivity of the protonated amine and compare its reactivity with the two reagents with those obtained from halogenation of the quaternary salt. The results obtained are given in Table IV.

Table III. Relative Reactivities/H in the Chlorinations of n-Butyltrimethylammonium Chloride, n-Pentyltrimethylammonium Chloride, and n-Hexyltrimethylammonium Chloride with N-Chlorodimethylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$.[a]

| Reaction # | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ |
|---|---|---|---|---|---|---|
| 7 | 0.0[b] (0)[d] | 0.0 (0) | 0.31±0.03[c] (4.8) | 4.6±0.3 (72) | 1.0 (23) | |
| | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ |
| 8 | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.54±0.17 (3.2) | 15.1±1.5 (88) | 1.0 (8.8) |
| | $(CH_3)_3\overset{\oplus}{N}$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$—$CH_3$ |
| 9 | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 2.3±0.1 (11) | 18.0±1.4 (83) | 1.0 (6.9) |

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
c. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
d. (Percent yield), based on total products formed.

Table IV. Relative Reactivities/H in the Chlorination of n-Pentyldimethylamine with Molecular Chlorine or N-Chlorodimethylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$.[a]

| Reaction # | Chlorinating Reagent | $(CH_3)_2N$—$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ |
|---|---|---|---|---|---|---|---|
| 10 | $Cl_2$ | 0.0[b] (0)[d] | 0.0 (0) | 0.0 (0) | 1.3±0.2[c] (21) | 3.3±0.7 (54) | 1.0 (25) |
| 11 | $(CH_3)_2NCl$ | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0)) | 12.7±0.9 (89) | 1.0 (11) |

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
c. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
d. (Percent yield), based on total products formed.

The Photochlorinations of N-Chloromethyl-n-pentylamine and N-Chloromethyl-n-hexylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$ - The Hofmann-Löffler-Freytag reaction has been proposed to proceed by the intramolecular hydrogen abstraction of an amminium radical, in cases where the nitrogen atom can abstract in a 5, 6 or 7 membered cyclic transition state.[5] Since a method was now available for analysis of the products without the complications arising from treatment with base, these reactions were reinvestigated.

N-chloroamines **5** and **6** were prepared from the corresponding amines by the procedure of Coleman,[4] and photolyzed at 30°C in 15% $CD_3CO_2D$/85% $H_2SO_4$ with incandescent light. The reactions were qualitatively faster than the chlorinations of the quaternary salts with N-chlorodimethylamine, taking less than 24 hours to complete. The product mixtures obtained were analyzed by NMR, and the results obtained are given in Table V.

Table V. Relative Reactivities/H in the Self Chlorinations of N-Chloro-n-pentylmethylamine and N-Chloro-n-hexylmethylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$.[a]

| Reaction # | $CH_3$—N(Cl)—$CH_2$ | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_3$ |
|---|---|---|---|---|---|---|
| 12 | 0.0[b] (0)[d] | 0.0 (0) | 0.0 (0) | 0.33±0.10[c] (0.25) | 129±11 (99) | 1.0 (1.1) |
| | $CH_3$—N(Cl)— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$— | —$CH_2$—$CH_3$ |
| 13 | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 115±5 (81) | 25.5±0.7 (18) | 1.0 (1.1) |

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
c. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
d. (Percent yield), based on total products formed.

Control Experiments - To ensure that the N-chlorodimethylamine prepared here was of the same purity as that prepared by Ingold,[32] the chlorination of 1-chlorobutane in 15% $CH_3CO_2H$/85% $H_2SO_4$ with N-chlorodimethylamine was carried out. The reaction mixtures were diluted with $H_2O$ and extracted into $CCl_4$. Freon 112 was used as an internal standard and the product yields were determined by glpc analysis. The product ratios obtained from these reactions was identical, within the experimental reproducibility listed for the analytical NMR method, to those reported previously.[32]

The reliability of the analytical procedure used and the stability of the reaction products in the two solvent systems were also confirmed by subjecting synthetic mixtures of known composition of the chlorination products of the quaternary ammonium salt **2**, to analysis after they had been exposed to the reaction conditions. The errors presented in Tables I-V appear to be within the limits of these analytical determinations.

In all of the analyses presented in Tables I-V no unidentified absorbance signals were detected. These observations insured that within the experimental limits only the chlorinated products reported were produced.

## DISCUSSION

The effect of solvent and radical reactivity on isomer distributions in the absence of polar effects could be examined in the usual manner by a comparison of the product yields obtained from the chlorination of 2,3-dimethylbutane under the reaction conditions. The relative reactivities calculated from the product ratios obtained from the chlorinations of 2,3-dimethylbutane with molecular chlorine, in the solvent systems used, compared well with those reported in the literature for chlorinations in an inert solvent, 2,3-dimethylbutane.[34] Furthermore the tertiary/primary selectivities/H for the chlorinations (hexachloroacetone, 4.0:1; 85% $H_2SO_4$/15% $CH_3CO_2H$, 3.3:1; neat, 4.2:1) with molecular chlorine were essentially the same as that reported by Deno[35] for the chlorination of that substrate with N-chlorodimethylamine (30% $H_2SO_4$, 3.8:1). The effects of both solvent and reagent on the relative reactivity of an intramolecular competitive chlorination are more readily seen in the results of the study of the chlorination of 1-chlorobutane (see Table VI). The solvent does not appear to greatly affect the distribution of products from the reactions of the neutral species (2,3-dimethylbutane, 1-chlorobutane) with molecular chlorine, while a significant affect was observed for the N-chloroamine chlorinations of 1-chlorobutane. This observation confirmed the original results reported by Ingold[32] and further assured that our preparation of the reagent, by their method, underwent reaction by a chain mechanism whose chain carrier, an ammonium radical, was significantly different from the chlorine atom.

Table VI. The Relative Reactivities/H from the Photoinitiated Chlorination of 1-Chlorobutane (30°C).[a]

| Reagent | Solvent | Cl—$CH_2$— | ——$CH_2$— | ——$CH_2$— | ——$CH_3$ | Ref. |
|---|---|---|---|---|---|---|
| $Cl_2$ | neat | 0.54 (6.7) | 1.9 (23.6) | 4.1 (51.0) | 1.0 (18.6) | 38 |
| $Cl_2$ | $H_2SO_4/HO_2CCH_3$ | 0.38 (5.4) | 1.5 (20.9) | 3.6 (52.0) | 1.0 (21.6) | 28 |
| $(CH_3)_2NCl$ | $H_2SO_4/HO_2CCH_3$[b] | 1.2 (4.8) | 2.7 (10.6) | 20.4 (78.8) | 1.0 (5.8) | 32 |
| $(CH_3)_2NCl$ | $H_2SO_4/HO_2CCH_3$ | 0.75 (4.1) | 1.4 (7.7) | 14.6 (80.0) | 1.0 (8.2) | This work |

a. Values in parenthesis are (Percent Yield), based on total products found.
b. AIBN initiated, 4 M $H_2SO_4/CH_3CO_2H$.

The isomer distribution for the chlorinations of substituted butanes has been rationalized as being due to a polar deactivation of the carbon-hydrogen bond closest to the electronegative substituent.[28,36-38] The effect presumably falls off with the distance from the substituent. The polar effects appear to control the product distribution since the ease of abstraction, in opposition to

the polar influences, would favor substitution at the α then β followed by the γ and lastly the δ positions. The selectivity of the abstracting radical influences the distribution of the products by favoring abstraction at the more reactive position. In the comparison of the reactions of several radicals with substrates where the opposing effects are operative the most reasonable measure of the selectivity is the ratio of $(\omega_{-1})/(\omega)$. As is seen in Table VI the $(\omega_{-1})/(\omega)$ ratio is larger for the positively charged amminium radical than for the chlorine atom and argues that with an even greater polar effect the selectivity of the radical shows an even greater preference to secondary/primary hydrogen abstraction. However, since the 1-chlorobutane will show a pronounced deactivation to abstraction by the nitrogen radical cation the rate of chlorination by the N-chloroamine would be expected to be slower than the rate of chlorination with molecular chlorine. This expectation, at least qualitatively, was confirmed since instead of the usual 1 hr irradiation necessary for the chlorination reactions with molecular chlorine, the N-chloroamine reactions required >20 hr irradiation for complete reaction.

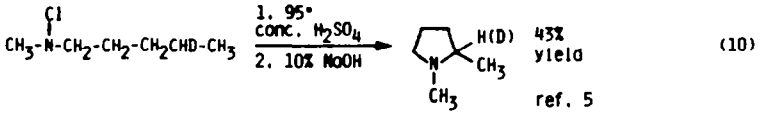
The chlorination of the quaternary ammonium salts with molecular chlorine in either solvent, hexachloroacetone or $H_2SO_4/CH_3CO_2H$, showed a similar but even more pronounced deactivation (>6 hr irradiation for complete reaction) due to the more strongly deactivating influence of the full positive charge resident on the substituent. The influence of the positive charge is reflected by the product distribution (see Tables I-II). Deactivation appears to extend significantly for three carbons removed from the quaternary center (see, reactions 2-3, Table I). In the more polar solvent (see Table II) the polar effect is more pronounced, presumably since charge separation inherent in the transition state is more easily supported in the acidic solvent. Qualitatively the solvent effect is seen upon examination of the ratio $\Sigma\ (\omega_{-2} + \omega_{-1})/\omega$ in Table I, reactions 2, 3 and Table II, reactions 5 and 6. In hexachloroacetone the ratio is > 4-4.5 while in $H_2SO_4/CH_3CO_2H$ it is < 1.5.

The isomer distribution found for the chlorinations with N-chlorodimethylamine in $H_2SO_4/CH_3CO_2H$ (Table III) are markedly different than those carried out in the same solvent with molecular chlorine. Since the abstracting species is most probably the protonated amminium radical, the effects upon the isomer distribution should reflect an enhanced polar effect and an enhanced selectivity. As predicted for the more stable, less reactive ammonium radical, $\Sigma(\omega_{-1} + \Delta_{-2})/\omega$, gives a higher selectivity, higher ratio, and a more pronounced polar deactivation since the $(\omega_{-2})$ position shows a greatly diminished reactivity compared with that found using molecular chlorine. Consistent with a highly deactivated chain reaction between a positively substituted alkane and a positively charged amminium radical, the reaction took > 120 hr of irradiation to reach completion.

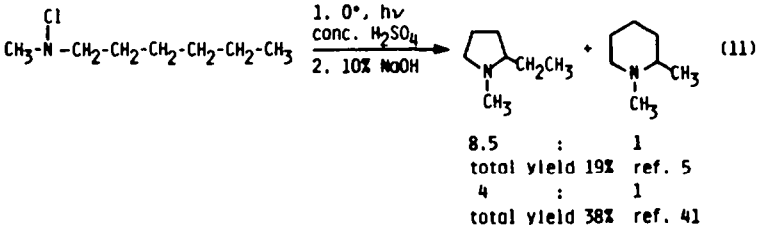
Although we have attempted to use the tetraalkylammonium salt as a model for the substrate (the protonated N-chloroamine) which undergoes substitution, if the HLF reaction proceeds by an intermolecular substitution, another possible model would be the protonated trialkylamine. The chlorination of this substrate with molecular chlorine displays an apparently less pronounced polar effect ($\Sigma\ (\omega_{-1} + \omega_{-2})/\omega = 3$) then the quaternary ammonium salt. The difference may be, however, due to the intramolecular reaction of some N-chloro-n-pentyldimethylamine, formed from reaction with the chlorine, since this reaction has been documented previously.[39] When N-chlorodimethylamine was the chlorinating agent (the dimethylammonium radical cation acting as the chain carrier) the distribution of products was almost the same for the two substrates. These observations suggest that abstraction from the unprotonated amine during the HLF reaction is not an

important process, contrary to a previous suggestion.[40] Presumably any inductive difference between the tetraalkylammonium salt and the trialkylammonium salt becomes insignificant when the abstracting species is the positively charged radical cation.

Intramolecular vs Intermolecular Abstraction - In their mechanistic studies both Wawzonek[41] and Corey[5] investigated the products obtained from the (HLF) reaction of VI, while Corey and Hertler[5] also investigated the products from the 4-deuterio analog of N-chloroamine 5. The results they obtained are shown below (equations 10 and 11). The yields of products were poor and differed considerably, however, both groups concluded that hydrogen transfer occurred through an intramolecular abstraction (equation 12) rather than an intermolecular abstraction (equation 13).

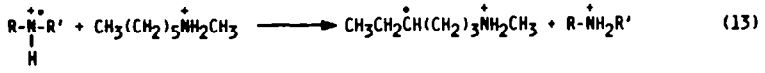



(10)




(11)

(12)



(13)

Both reports noted that residual unidentified material remained after the cyclized products were isolated. During the treatment with sodium hydroxide those chlorinated amines which are not sterically prevented from doing so, cyclize. Chlorinated amines which do not readily cyclize, and some of those which are capable of cyclizing, are never isolated since they polymerize to high molecular weight products.

For the intermolecular reactions of N-chlorodimethylamine with the quaternary salts three abstracting species are possible intermediates: the chlorine atom, the amino radical, or the amminium radical. For reactions of N-chloroamines 5 and 6 not only the three abstracting species need be considered, but also the nature of the substrate. The possible mechanisms for the self chlorination reactions of 5 and 6 are divided into two classes depending upon whether the hydrogen abstraction is intramolecular or intermolecular.

It has been argued that for the concentrations involved the unprotonated N-chloroamines and/or amines can be neglected from consideration as reactants and the amino radical can most likely be eliminated as an abstracting species for an intermolecular abstraction.[42]

In the case of a intermolecular reaction the protonated N-chloroamine would most likely serve as substrate in the initial stages of the reaction, while the protonated amine (formed from reaction with HCl) would compete at the end of the

reaction. The product distributions obtained from the reactions of the N-chloroamines (see Table V) are very different from those obtained from the chlorination of the quaternary salts, with molecular chlorine (reactions 5 and 6, Table II). This observation eliminates the chlorine atom from consideration as the abstracting species in an intermolecular process.

Comparison of reaction 12 (Table V) with reaction 11 (Table IV) or reaction 8 (Table III), assuming the small differences are due to the different N-chloroamines used, would suggest that an intermolecular abstraction by the amminium radical could be responsible for the relatively specific reactivities observed in the supposedly intramolecular reactions. However, comparison of reaction 13 (Table V) with reaction 9 (Table III), is strong evidence for intramolecular hydrogen abstraction, since the 4-chloroproduct (the product from a six-membered internal abstraction transition state) is still the major product resulting from the reactions of N-chloroamine **6**. Since it is unlikely that N-chloroamines **5** and **6** should react by different mechanisms, it can be concluded that both substrates react by an intramolecular hydrogen abstraction.

The results obtained from the reaction of N-chloroamine **5** (see Table V) indicate a yield of 99% of the N-methylpyrrolidine, if cyclization were 100% efficient. The products of the self chlorination of N-chloroamine **6** indicate a theoretical yield of 81% for 2-ethyl-1-methylpyrrolidine and 18% of 1,2-dimethylpiperidine if cyclization were 100% efficient. All of the previously reported yields (equations 25 and 26) are lower, and the ratio of the pyrrolidine to piperidine obtained from N-chloroamine **6** reported by Corey,[5] was larger than those suggested from the values listed in Table V. These differences in results are most likely due to the isolation steps, during which cyclization of the chlorinated amine occurs. Wawzonek[41] obtained a higher yield of isolated products than Corey,[5] and also obtained a similar ratio of the pyrrolidine to the piperidine as those predicted from the results listed in Table V. These observations support the suggestion that the discrepancies in product yield are due to inefficient isolation of products.

Mechanistic Conclusions - On the basis of the complete product studies obtained by the NMR analysis presented in this work the intramolecular abstraction mechanism of Wawzonek[7] still best explains the product determining reaction of the HLF reaction.

In contrast with the conclusions of Ingold[32] and Tanner,[28] on the mechanism of the intermolecular analog, the intramolecular reactions do not appear to be sensitive to the method used to prepare the reagent.

The selectivities[5,11], previously reported were obtained from reactions which gave low yields of products and are most likely the result of incomplete cyclization after the treatment with strong base.

## EXPERIMENTAL

### Materials

Hexachloroacetone (Eastman) was distilled at 28-32°C at 0.3 mm Hg pressure through an 8" Vigreux column. 400 MHz $^1$H NMR spectrometry showed it to contain no observable protons.

Carbon tetrachloride (Fisher Scientific Co.) was distilled over $P_2O_5$ before use. Glpc analysis showed it to be >99.9% pure.

Sulfuric acid (Fisher Scientific Co.), Perdeuterioacetic acid (99.5% D Fisher Scientific Co.), Perdeuterioacetonitrile (99% D Merck Sharp and Dohme Canada Limited), 2,3-dimethylbutane (Phillips Petroleum Company, Research Grade >99.88%) were used without further purification.

Chlorine (Matheson) was distilled and bubbled through concentrated sulfuric acid, and sodium hydroxide pellets.

1-Chlorobutane (Matheson Coleman and Bell) was distilled through an 18" Vigreux column. Glpc analysis showed it to be >99.9% pure.

## Instrumentation

NMR spectra,400 MHz $^1H$, were obtained using a Bruker WH-400 NMR spectrometer; 90 MHz $^1H$ NMR spectra were obtained with a Perkin-Elmer R32 NMR spectrometer, and 60 MHz $^1H$ NMR spectra were obtained using a Varian A-56/60A NMR spectrometer. Glpc analyses were obtained using a Carlo Erba Fractovap Mod. GV gas chromatograph equipped with a flame ionization detector. The product mixtures were quantitatively measured using a calibration mixture of the authentic materials plus the standard used. Mass spectra were run with an AEI model MS12 mass spectrometer. Ultraviolet spectra were obtained with a Unicam SP1700 ultraviolet spectrophotometer.

## Quaternary Ammonium Salts

The ammonium salts were prepared from the appropriate 1-chloroalkane and trimethylamine according to the procedure of Smith and Frank.[43] The chloroalkane was dissolved in methanol containing trimethylamine and the mixture was sealed in a thick walled reaction tube and heated to 60°C for 24 hr. The solvent was removed by vacuum distillation and the white solid was washed with ether and dried under vacuum at 60°C. The chlorinated ammonium salts were prepared by nucleophilic displacement of the primary chloride from the appropriate chlorinated primary chloride. When 1,4-dichloropentane, 1,3-dichloropentane, 1,6-dichlorohexane, 1,5-dichlorohexane, 1,4-dichlorohexane and 1,3-dichlorohexane were used as the reagent the reactions were carried out at 50°C. When the methanol was removed the oily solid was dissolved in methylene chloride and reprecipitated by the addition of diethyl ether or dissolved in water, washed with methylene chloride and the water removed by distillation at reduced pressure and dried under vacuum over $P_2O_5$.

n-Butyltrimethylammonium chloride: mp 225-230°C (dec.), (lit.[44] mp 223.7-224°C); 400 MHz $^1H$ NMR data ($CD_3CN$) δ 1.00 (t, J = 7 Hz, 3H), 1.43 (m, 2H), 1.81 (m, 2H), 3.15 (s, 9H), 3.36 (m, 2H).

n-Pentyltrimethylammonium chloride[45]: mp 197-199°C; 400 MHz $^1H$ NMR data ($CD_3CN$) δ 0.95 (t, J = 7 Hz, 3H), 1.40 (m, 4H), 1.83 (m, 2H), 3.15 (s, 9H), 3.35 (m, 2H).

n-Hexyltrimethylammonium chloride[46]: mp 197-197.5°C; 400 MHz $^1H$ NMR data ($CD_3CN$) δ 0.995 (t, J = 5 Hz, 3H), 1.46 (m, 6H), 1.85 (m, 2H), 3.15 (s, 9H), 3.30 (m, 2H).

4-Chloro-n-butyltrimethylammonium chloride: mp 148-151°C; 400 MHz $^1H$ NMR data δ 1.90 (m, 2H), 2.01 (m, 2H), 3.17 (s, 9H), 3.41 (m, 2H), 3.72 (t, J = 6 Hz, 2H); mass spectrum m/e (rel intensity) 100 (0.3), 59 (10.7), 58 (100), 50 (35.0), 42 (25.3).
Anal. Calcd for $C_7H_{17}Cl_2N$: C, 45.17; H, 9.21; N, 7.53. Found: C, 44.77; H, 9.38; N, 7.79.

5-Chloro-n-pentyltrimethylammonium chloride: mp 115-116°C; 400 MHz $^1H$ NMR data ($CD_3CN$) δ 1.56 (m, 2H), 1.88 (m, 4H), 3.15 (s, 9H), 3.37 (m, 2H), 3.68 (t, J = 7 Hz, 2H); mass spectrum m/e (rel intensity) 151 (0.2), 149 (0.7), 114 (1.4), 59 (5.4), 58 (89.3), 42 (11.7), 36 (100).
Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.57; N, 7.00. Found: C, 48.37; H, 9.67; N, 7.32.

4-Chloro-n-pentyltrimethylammonium chloride: mp 131-133°C; 400 MHz $^1H$ NMR data ($CD_3CN$) δ 1.52 (d, J = 7.2 Hz, 3H), 1.79 (m, 2H), 1.98 (m, 2H), 3.13 (s, 9H), 3.36 (m, 2H), 4.23 (m, 1H); mass spectrum m/e (rel intensity) 149 (0.1), 114 (0.1), 113 (1.1), 59 (6.3), 58 (100), 50 (17.6), 42 (15.1).
Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.57; N, 7.00. Found: C, 47.79; H, 9.57; N, 7.05.

3-Chloro-n-pentyltrimethylammonium chloride: mp 154-155°C; 400 MHz $^1H$ NMR data ($CD_3CN$) δ 1.01 (t, J = 7.2 Hz, 3H), 1.81 (m, 2H), 2.21-2.33 (m, 2H), 3.15 (s, 9H), 3.49 (d of t, J = 12, 3.6 Hz, 1H), 3.65 (d of t, J = 12, 3.6 Hz, 1H); 4.04 (m, 1H); mass spectrum m/e (rel intensity) 114 (0.2), 113 (1.3), 59 (9.6), 58 (100), 50 (11.4), 42 (21.0).
Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.57; N, 7.00. Found: C, 47.98; H, 9.50; N, 6.99.

6-Chloro-n-hexyltrimethylammonium chloride: mp 92-93°C; 200 MHz $^1H$ NMR data ($CD_3CN$) δ 1.24-1.57 (m, 4H), 1.74 (m, 4H), 3.06 (s, 9H), 3.27 (m, 2H), 3.59 (t, J = 6 Hz, 2H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (3.9), 180 (37.4), 179 (12.3), 178 (100), 144 (5.5).

5-Chloro-n-hexyltrimethylammonium chloride: mp 64-65°C; 200 MHz $^1H$ NMR data ($CD_3CN$) δ 1.48 (d, J = 6 Hz, 3H), 1.73 (m, 6H), 3.12 (s, 9H), 3.37 (m, 2H), 4.12

(m, 1H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (3.5), 180 (34.3), 179 (11.3), 178 (100), 144 (3.5).

4-Chloro-n-hexyltrimethylammonium chloride: mp 117-120°C; 200 MHz $^1$H NMR data ($CD_3CN$) δ 1.00 (t, J = 7 Hz, 3H), 1.75 (m, 4H), 2.02 (m, 2H), 3.05 (s, 9H), 3.29 (m, 2H), 3.96 (m, 1H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (3.6), 180 (33.9), 179 (11.3), 178 (100), 144 (5.0).

3-Chloro-n-hexyltrimethylammonium chloride: mp 112-114°C; 200 MHz $^1$H NMR data ($CD_3CN$) δ 0.95 (t, J = 7 Hz, 3H), 1.49 (m, 2H), 1.77 (m, 2H), 1.85 (m, 2H), 3.19 (s, 9H), 3.58 (m, 2H) 4.05 (m, 1H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (4.0), 180 (38.7), 179 (12.9), 178 (100), 144 (10.0).

The N-chloromethylammonium salts were prepared by the same method in methanol at 50°C, by allowing n-pentydimethylamine, n-hexyldimethylamine and n-butyldimethylamine to react with methylene chloride.

n-Butylchloromethyldimethylammonium chloride: mp 108-110°C; 200 MHz $^1$H NMR data ($CD_3CN$) δ 1.06 (t, J = 7 Hz, 3H), 1.45 (sext., J = 8 Hz, 2H), 1.81 (m, 2H), 3.36 (s, 6H), 3.62 (m, 2H), 5.65 (s, 2H); fast atom bombardment mass spectrum m/e (rel intensity) 153 (3.1), 152 (37.8), 151 (9.9), 150 (100), 116 (11.1). Anal. Calcd for $C_7H_{17}Cl_2N$: C, 45.17; H, 9.21. Found: C, 45.22; H, 9.16.

n-Pentylchloromethyldimethylammonium chloride: mp 57-57.5°C; 200 MHz $^1$H NMR data ($CD_3CN$) δ 1.02 (t, J = 8 Hz, 3H), 1.45 (m, 4H), 1.83 (m, 2H), 3.38 (s, 6H), 3.62 (m, 2H), 5.68 (s, 2H); fast atom bombardment mass spectrum m/e (rel intensity) 167 (3.1), 166 (33.1), 165 (9.9), 164 (100), 130 (14.1). Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.59. Found: C, 48.39; H, 9.95.

n-Hexylchloromethyldimethylammonium chloride: mp 72-74°C; 200 MHz $^1$H NMR data ($CD_3CN$) δ 1.01 (t, J = 7 Hz, 3H), 1.45 (m, 6H), 1.83 (m, 2H), 3.40 (s, 6H), 3.64 (m, 2H), 5.74 (s, 2H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (3.8), 180 (36.0), 179 (12.0), 178 (100), 144 (20.6). Anal. Calcd for $C_9H_{21}Cl_2N$: C, 50.47; H, 9.88. Found: C, 50.70; H, 9.96.

## Amines

n-Pentyldimethylamine: n-pentyldimethylamine was prepared from 1-bromopentane and dimethylamine with sodium carbonate in 50:50 methanol:water v:v, at 60°C. The solution was extracted with diethyl ether and the extracts were dried over anhydrous sodium sulfate. The product was isolated by fractional distillation to yield a clear liquid: bp 118-122°C (692 mm) [lit.[47] bp 123°C]; $n_D^{20}$ = 1.4081 [lit.[47] $n_D^{20}$ = 1.4083]; 90 MHz $^1$H NMR data ($CD_3CN$) δ 0.90 (t, J = 7 Hz, 3H), 1.33 (m, 6H), 2.20 (s, 8H).

n-Pentylmethylamine: n-pentylmethylamine was prepared from 1-bromopentane and methylamine with sodium carbonate in water. The solution was extracted with diethyl ether and the extracts were dried over anhydrous sodium sulfate. The product was isolated by fractional distillation to yield a clear liquid: bp 47-49°C (60 mm) [lit.[48] 45-47°C (60 mm)]; 400 MHz $^1$H NMR data ($CD_3CN$) δ 0.72 (t, J = 7 Hz, 3H), 1.19 (m, 4H), 1.54 (m, 2H), 2.69 (d, J = 6 Hz, 3H), 2.95 (m, 2H), 5.97 (broad m, 1H) [lit.[48] δ 0.6 (s, 1H), 0.75-1.08 (m, 3H) 1.16-1.5 (m, 6 H), 2.38 (s, 3H), 2.4-2.72 (m, 2H)].

n-Hexylmethylamine: n-hexylmethylamine was prepared from 1-bromohexane and methylamine with sodium carbonate in methanol:water 3:2 v:v, at 60°C. The solution was extracted with diethyl ether and the extracts were dried over sodium sulfate. The product was isolated by fractional distillation to yield a clear liquid: bp 32°C (4.7 mm) [lit.[41] 138-140°C (760 mm)]; $n_D^{20}$ = 1.4184 [lit.[41] $n_D^{20}$ = 1.4186); 400 MHz $^1$H NMR data ($CD_3CN$) δ 0.69 (t, J = 7 Hz, 3H), 1.14 (m, 6H), 1.53 (m, 2H), 2.69 (d, J = 6 Hz, 3H), 2.94 (m, 2H), 5.97 (broad m, 1H).

## N-Chloroamines

N-Chlorodimethylamine: N-chlorodimethylamine was prepared following the procedure of Ingold.[32] Dimethylamine and 6% aqueous sodium hypochlorite were mixed together. The solution was extracted with diethyl ether, washed with water, and dried over sodium sulfate. A slight excess of concentrated sulfuric acid (based on the dimethylamine used) was added and the ether was evaporated under vacuum in the dark. The resulting white crystals obtained were dissolved in an aliquot of 15% $CD_3CO_2D$/85% $H_2SO_4$ and stored in the dark at -78°C.

N-Chloro-n-hexylmethylamine and N-Chloro-n-pentylmethylamine: N-chloro-n-hexylmethylamine and N-chloro-n-pentylmethylamine were prepared by the method of Coleman.[4] The amine was stirred in a 50:50 mixture of ligroin and 3M aqueous sodium hydroxide (v:v) at 0°C. Chlorine was added at such a rate as to maintain a positive pressure of 40 mm Hg. When fuming had ceased and the ligroin solution had turned faintly green, the chlorine flow was stopped and the ligroin layer was separated. The ligroin was washed with ice cold fractions of 3 N sodium hydroxide, water and 2 N sulfuric acid. The ligroin layer was allowed to sit for 10 minutes in 15% $CD_3CO_2D$/85% $H_2SO_4$ while kept ice cold, and another 20 minutes with occasional stirring. This solution was then immediatedly used in the chlorinations.

Photochlorination Reactions

Photochlorination of Quaternary Ammonium Salts in Hexachloroacetone: Aliquot portions, 5 mL, of hexachloroacetone solutions 0.012-0.018 M in the salt and 0.0024-0.0035 in molecular chlorine were placed in pyrex ampoules, degassed, sealed, thermostated (30°C), and irradiated (2 x 100 watt) with incandescent light. After irradiation the tubes were opened and the solvent removed by vacuum distillation. Weighed amounts of naphthalene were added, the samples were dissolved in perdeuterioacetonitrile and analyzed by NMR spectroscopy.

Photochlorination of Quaternary Ammonium Salts and n-Pentyldimethylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$ with Molecular Chlorine: Aliquot portions of solutions of chlorine (0.068 M) and the salt (0.23-0.34 M) or amine (0.33 M) in the acid solvent was placed in pyrex reaction ampoules were degassed, sealed, equilibrated at 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened, o-dimethoxybenzene (weighed amounts) was added, and the samples analyzed by NMR spectroscopy.

Photochlorination of Quaternary Ammonium Salts and n-Pentyldimethylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$ with N-Chlorodiemthylamine: Aliquot portions of acid solutions of N-chlorodimethylamine (0.050 M), the salt (0.36 M) or the amine (0.36 M) were placed in pyrex ampoules, degassed, sealed, equilibrated to 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened and weighed amounts of o-dimethoxybenzene were added, and the samples analyzed by NMR spectroscopy.

Photochlorination of N-Chloro-n-pentylmethylamine and N-Chloro-n-hexylmethylamine in 15% $CD_3CO_2D$/85% $H_2SO_4$: Aliquot portions of acid solutions of N-chloroamine (0.62-0.70 M) were placed in pyrex reaction ampoules, degassed, sealed, equilibrated to 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened and weighed amounts of o-dimethoxybenzene were added, and the samples analyzed by NMR spectroscopy.

Photochlorination of 1-Chlorobutane with N-Chlorodimethylamine in 15% $CH_3CO_2H$/85% $H_2SO_4$: Aliquot portions of 1-chlorobutane (0.62 M) and N-chlorodimethylamine (0.089 M) in the acid solvent were placed in pyrex ampoules, degassed, sealed, equilibrated to 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened, added to ice-cold water and extracted with carbon tetrachloride. A standard solution of 1,5-dichloropentane in carbon tetrachloride was added and the mixture analyzed by Glpc. Glpc analysis was carried out using a 1/4" x 20' glass column of 5% SE 30 on Chromosorb W (30-120°C). The products were identified by a comparison of their retention times with those of authentic materials and the yields determined using the standard 1,5-dichloropentane. The absolute quantities were determined using standard calibration curves obtained from the analysis of mixtures of known composition.

The Photochlorination of 2,3-Dimethylbutane in Hexachloroacetone and Carbon Tetrachloride with Molecular Chlorine: A solution of 2,3-dimethylbutane (1.0 M), solvent and Freon 112 (0.21 M, gc standard) and molecular chlorine (0.18 M) and aliquot samples were placed in pyrex reaction ampoules. The ampoules were degassed, sealed, equilibrated to 30°C and exposed to light. After irradiation the tubes were opened, and analyzed by Glpc.

Glpc analysis was carried out using a 1/4" x 20' glass column of 10% Ucon 50 HB5100 on Chromosorb WAW (80°C). The products were identified by comparison of their retention times with those of authentic materials and the yields determined by using the standard Freon 112.

The Photochlorination of 2,3-Dimethylbutane in 15% $CH_3CO_2H$/85% $H_2SO_4$ with Molecular Chlorine: Aliquot samples of 2,3-dimethylbutane (0.61 M) and chlorine (0.056 M) in 15% $CH_3CO_2H$/85% $H_2SO_4$ were placed in pyrex reaction ampoules. The ampoules were degassed, sealed, equilbrated to 30°C and irradiated for the requisite amount of time. After irradiation the tubes were frozen, opened and diluted with ice-cold water. The aqueous solution was extracted with $CCl_4$ and the $CCl_4$ solution was analyzed by Glpc as described for the reactions in hexachloroacetone and $CCl_4$.

Product Stability Experiment: n-Pentyltrimethylammonium chloride was chlorinated in hexachloroacetone at 30°C and analyzed as described previously.

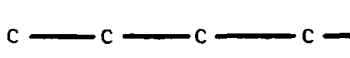
The NMR solvent ($CD_3CN$) was allowed to evaporate and each sample was dissolved in the appropriate amount of 15% $CD_3CO_2D$/85% $H_2SO_4$ and placed in stoppered pyrex flasks. The flasks were irradiated at 30°C for the same length of time as was used for the chlorination reactions carried out in the acid solvent. The mixtures were reanalyzed as described previously. Within the limits of the experimental error (±5%) the ratio of products were unchanged.

Product Identification and Measurements

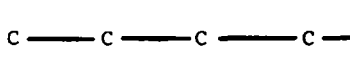
The product mixtures were analyzed by 400 MHz $^1H$ NMR spectrometry. For reactions run in hexachloroacetone, naphthalene was added as a standard before analysis. For reactions run in 15% $CD_3CO_2D$/85% $H_2SO_4$, o-dimethoxybenzene was used as a standard.

The yields of products were determined by measurement of the intensity of the absorption signals indicated in Table VII. The chemical shifts were assigned from the spectra mixtures of authentic products or by comparison to the spectra of similar products.

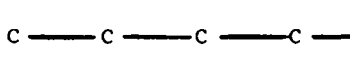
Table VII. Location of Chlorine Atom.



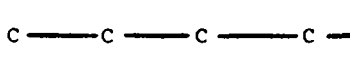
| | | | | | | |
|---|---|---|---|---|---|---|
| Shift (ppm) | 3.72 | 1.57 | 1.08 | 5.85-6.25[a] | 5.65 | (Salt 1) |
| Type | t[b] | d | t | m | s | |
| Location measured | C4 | C4 | C4 | C1 | CN | |



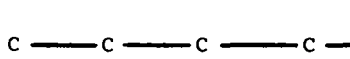
| | | | | | | |
|---|---|---|---|---|---|---|
| Shift (ppm) | 3.68 | 1.52 | 1.01 | 4.33-4.73[a] | 5.75-6.15[a] | 5.68 (Salt 2) |
| Type | t | d | t | m | m | s |
| Location measured | C5 | C5 | C5 | C2 | C1 | CN |



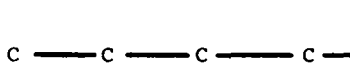
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Shift (ppm) | 3.59 | 1.48 | 1.05 | 4.05 | 4.35-4.75[a] | 5.80-6.20[a] | 5.74 (Salt 3) |
| Type | t | d | t | m | m | m | s |
| Location measured | C6 | C6 | C6 | C3 | C2 | C1 | CN |



| | | | | | | |
|---|---|---|---|---|---|---|
| Shift (ppm) | 3.45 | 1.39 | 0.86 | 4.06-4.46 | 5.46-5.86 | 5.29 (amine 4) |
| Type | t | d | t | m | m | d |
| Location measured | C5 | C5 | C5 | C2 | C1 | CN |



| | | | | | | |
|---|---|---|---|---|---|---|
| Shift (ppm) | 3.45 | 1.39 | 0.87 | 4.04-4.44 | 5.45-5.85 | 5.22 (amine 5) |
| Type | t | d | t | m | m | t |
| Location measured | C5 | C5 | C5 | C2 | C1 | CN |



| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Shift (ppm) | 3.44 | 1.35 | 0.86 | 3.86 | 4.03-4.43 | 5.44-5.84 | 5.28 (amine 6) |
| Type | t | d | t | m | m | m | t |
| Location measured | C6 | C6 | C6 | C3 | C2 | C1 | CN |

a. No authentic material was available for comparison. The shift given was estimated based on the shift observed for chlorination at other locations.
b. t, d, s and m signify triplet, doublet, singlet and multiplet respectively.

## REFERENCES


1. D.D. Tanner, D.W. Reed, B.P. Setiloane, J. Am. Chem. Soc. **1982**, 104, 3917.
2. Taken in part from the Ph.D. dissertation of C.P. Meintzer, University of Alberta, 1984.
3. Wolff, M.E. Chem. Rev. **1963**, 63, 55.
4. Coleman, G.H.; Nichols, G.; Martens, T.F. Org. Syn. **1955**, Coll. Vol. 3, 159.
5. Corey, E.J.; Hertler, R.W. J. Am. Chem. Soc. **1960**, 82, 1657.
6. Coleman, G.H.; Carnes J.J. Proc. Iowa Acad. Sci. **1942**, 49 288.
7. Wawzonek, S.; Thelan P.J. J. Am. Chem. Soc. **1950**, 72, 2118.
8. Kerwin, J.F.; Wolff, M.E.; Owings, F.F.; Lewis, B.B.; Blank, B.; Magnani, A.; Karash C.; Georgian, V. J. Org. Chem. **1962**, 27, 3628.
9. Adam, G.; Schreiber, K. Tetrahedron. Lett. **1963**, 943 and Adam, G.; Schreiber, K. Tetrahedron **1964**, 20, 1719.
10. Van de Woude, G.; van Hove, L. Bull. Soc. Chim. Belg. **1975**, 84, 911.
11. Hofmann, A.W. Ber. **1885**, 18, 109.
12. Lellmann, E. Ann. **1890**, 259, 193.
13. Partch, R. Tetrahedron. Lett. **1966**, 1361.
14. Hertler, W.R.; Corey, E.J. J. Org. Chem. **1959**, 24, 572.
15. Gassman, P.G.; Heckert, D.C. Tetrahedron **1965**, 21, 2725.
16. Furstoss, R.; Teissier, P.; Waegell, B. Tetrahedron. Lett. **1970**, 1263.
17. Dupeyre, R-M.; Rassat, A. Tetrahedron. Lett. **1973**, 2699.
18. Kimura, M.; Ban, Y. Synthesis **1976**, 201.
19. Hofmann, A.W. Ber. **1883**, 16, 558, 586.
20. Löffler, K.; Freytag, C. Ber. **1909**, 42, 3427.
21. Löffler, K.; Kober, S. Ber. **1909**, 42, 3421.
22. Löffler, K. Ber. **1910**, 43, 2025.
23. Wawzonek, S.; Nelson, M.F., Jr.; Thelen, P.J. J. Am. Chem. Soc. **1951**, 73, 2806.
24. Minisci, F.; Galli, R.; Cecere, M. Tetrahedron. Lett. **1965**, 4663.
25. Minisci, F.; Galli, R.; Galli, A.; Bernardi, R. Tetrahedron. Lett. **1967**, 2207.
26. Minisci, F.; Galli, R.; Bernardi, R. Chem. Commun. **1967**, 903.
27. Bernardi, R.; Galli, R.; Minisci, F. J. Chem. Soc. (B) **1968**, 324.
28. Tanner, D.D.; Mosher, M.W. Can. J. Chem. **1969**, 47, 715.
29. Minisci, F.; Gardini, G.P.; Bertini, F. Can. J. Chem. **1970**, 48, 544.
30. Deno, N.C.; Billups, W.E.; Fishbein, R.; Pierson, C.; Whalen, R.; Wyckoff, J.C. J. Am. Chem. Soc. **1971**, 93, 438.
31. Deno, N.C.; Pohl, D.G. J. Org. Chem. **1975**, 40, 380.
32. Spanswick, J.; Ingold, K.U. Can. J. Chem. **1970**, 48, 546.
33. Minisci, F.; Bernardi, R.; Trabucchi, V.; Grippa, L. Chimica e Industria (Milan) **1966**, 48, 484.
34. G.A. Russell, J. Am. Chem. Soc. **1957**, 79, 2977.
35. Deno, N.C.; Fishbein, R.; Wyckoff, J.C. J. Am. Chem. Soc. **1971**, 93, 2065.
36. Fredricks, P.S.; Tedder, J.M. Chem. Ind. London, **1959**, 490.
37. Fredricks, P.S.; Tedder, J.M. J. Chem. Soc. **1960**, 144.
38. Tanner, D.D.; Van Bostelen, P. J. Org. Chem. **1967**, 32, 1517.
39. Deno, N.C. in "Methods in Free-Radical Chemistry", Vol. 3, E.S. Huyser, Ed., Dekker and Co., New York, **1972**, p. 135.
40. Tedder, J.M. Quart. Rev. (London) **1960**, 14, 336.
41. Wawzonek, S.; Culbertson, T.P. J. Am. Chem. Soc. **1960**, 82, 441.
42. Anson, P.C.; Fredericks, P.S.; Tedder, J.M. J. Chem. Soc. **1959**, 918.

43. Smith, P.A.S.; Frank, S. J. Am. Chem. Soc. **1952**, 74, 509.
44. Grovenstein, E., Jr.; Blanchard, E.P., Jr.; Gordon, D.A.; Stevenson, R.W. J. Am. Chem. Soc. **1959**, 81, 4842.
45. Nogrady, T.; Burgen, A.S.V. J. Am. Chem. Soc. **1969**, 91, 3890.
46. Kuznetsova, N.N.; Vansheidt, A.A.; Papukova, K.N.; Komyakova, T.N. Zh. Prikl. Khim. **1966**, 39, 1529.
47. "Handbook of Chemistry and Physics", 57th Ed., R.C. Weast, Ed., Chemical Rubber Company Press, Cleveland, **1976**, pp C-107.
48. Abatjoglou, A.G.; Eliel, E.L. J. Org. Chem. **1974**, 39, 3042.