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AN INVESTIGATION OF SOME SYNTHETICALLY USEFUL DECARBOXYLATION REACTIONS

by

DENNIS LIOTTA

A dissertation submitted to the
Graduate Faculty in Chemistry in
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Abstract

AN INVESTIGATION OF SOME SYNTHETICALLY USEFUL DECARBOXYLATION REACTIONS

by

DENNIS LIOTTA

Adviser: Professor Robert Engel

Two related investigations have been performed; in the first study the vapor phase thermal decomposition of alkoxycarbonyl thiocyanates and isothiocyanates over glass wool at 5 Torr and temperatures between 240° - 375° C has been investigated. The starting compounds were synthesized in a two step sequence by reaction of an alcohol with phosgene, followed by treatment of the resulting chloroformate with potassium thiocyanate. Pyrolysis of these compounds yielded mixtures of alkyl thiocyanates and isothiocyanates. Alkoxycarbonyl thiocyanates and isothiocyanates derived from simple primary alcohols yielded alkyl thiocyanates almost exclusively, while those derived from secondary and tertiary alcohols yielded mostly alkyl isothiocyanates. Since overall yields were high and no alkyl rearrangements were observed, this reaction has potential synthetic utility for the synthesis of primary alkyl thiocyanates (and the corresponding thiols) and secondary and tertiary isothiocyanates (and the corresponding amines and methyl

amines).

The fact that, for a given alkyl substituent, both isomers (alkoxycarbonyl thiocyanates and isothiocyanates) gave essentially the same product ratios upon pyrolysis strongly indicates that the decomposition of both isomers proceeds through a common intermediate. This fact, coupled with various other observed trends, indicates that this intermediate is most probably an intimate ion pair.

In the second study the reaction of α,N-diphenylnitrone with thionyl chloride and phosgene was investigated. In each case the reaction yielded the corresponding alkylidene *ortho*-chloroaniline hydrochloride almost exclusively (small amounts of the *para*- isomers were at times isolated). Chlorination proceeded exclusively on the N-aryl ring, even when the other aryl ring contained substituents highly activating for electrophilic aromatic substitution. This fact, coupled with the very high *ortho*:*para* ratios observed, indicates the reaction probably proceeds through a cyclic six-membered transition state.

Since these reactions proceeded rapidly and in high yield at room temperature, the applicability of this reaction as a general positional-selective method for the synthesis of *ortho*-chloro imines (and by hydrolysis the corresponding amines) appears to be quite exceptional.

The generality of the reaction with other N-aryl

nitrogen oxides has also been investigated. While *ortho*-chlorination is observed with N,N-dimethylaniline-N-oxide, various diaryl azoxy compounds yielded onyl deoxygenated product. Aryl nitroso compounds reacted with thionyl chloride or phosgene to yield 2,4-dichloroaniline, apparently *via* an N,N-dichloroaniline intermediate.

ACKNOWLEDGEMENTS

I would like to extend my sincere thanks to Professor Robert Engel for the very capable guidance which he gave me in my research. I would also like to thank Professors Norman L. Goldman and A. David Baker who also gave me much assistance and with whom I had many stimulating conversations. Finally I wish to thank Ms. Jan Silverman for her assistance in preparing and typing this thesis.

TO MY WIFE

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CHAPTER I

THERMAL DECOMPOSITION OF ROC(O)X SYSTEMS

1. Alkyl Chloroformates: Of the ROC(O)X systems which will be discussed here, alkyl chloroformates, ROC(O)Cl, have been the most thoroughly investigated. Although side products are often observed, the thermal decomposition of these compounds proceeds as shown below (equation 1):

$$\mathrm{ROC(O)Cl} \longrightarrow \mathrm{R\text{-}Cl} + \mathrm{CO_2} \qquad (1)$$

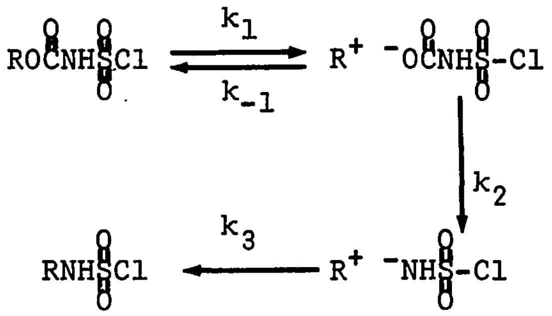
Originally this decomposition was thought to proceed *via* a simple S_Ni mechanism.[1] However, the large negative Hammett ρ constant obtained by Wiberg and Shryne[2] in a study of the thermal decomposition of substituted α-phenethyl chloroformates indicated a highly polar transition state.

The mechanistic details of this decomposition were further refined by Lewis and Herndon.[3] In a gas phase kinetic study using a flow system, they obtained first-order rate constants for the formation of both alkyl chloride and olefins. Furthermore, optically active *sec*-butyl chloroformate yielded *sec*-butyl chloride with complete retention of configuration and neopentyl chloroformate yielded neopentyl chloride and methylbutenes, but no *tert*-amyl chloride. On the basis of these data they proposed a "rather polar S_Ni mechanism" for the formation of alkyl chlorides from alkyl chloroformates. Although the data did not completely exclude a one-step, non-polar elimination reaction, it strongly indicated that olefins are formed via a transition state with a substantial degree of charge separation.

Clinch and Hudson[4] studied the thermal decomposition of alkyl chloroformates by means of gas-liquid chromatography. Not only were substantial alkyl rearrangements observed, but the total molar per cent of olefin obtained was often equal to or greater than that of the alkyl chlorides. These results were interpreted in terms of a substantially dissociated carbonium ion intermediate, and thus would tend to complement the results of Lewis and Herndon. since a larger degree of dissociation is possible in the liquid phase.

2. Chlorosulfonylurethanes: Chlorosulfonylurethanes, $ROC(O)NHS(O)_2Cl$, are prepared by allowing an alcohol to react with chlorosulfonyl isocyanate. The only study of the thermal decomposition of these compounds was reported by Hendrickson and Joffee.[5] The thermal decomposition was performed at temperatures slightly higher than room temperature. As with alkyl chloroformates, the primary process was decarboxylation, although substantial amounts of olefin were also obtained. The authors proposed the mechanism given in equation 2. The large amount of elimination was explained in terms of the longer lifetime and greater

basicity of $ClSO_2NH^-$, relative to Cl^-.



$$\mathrm{RO\overset{O}{C}NH\overset{O}{\underset{O}{S}}Cl} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R^+\ {}^-O\overset{O}{C}NH\overset{O}{\underset{O}{S}}\text{-}Cl} \xrightarrow{k_2} \mathrm{R^+\ {}^-NH\overset{O}{\underset{O}{S}}\text{-}Cl} \xrightarrow{k_3} \mathrm{RNH\overset{O}{\underset{O}{S}}Cl} \qquad (2)$$

3. <u>Other Systems</u>: Other systems of the type ROC(O)X for which the thermal decomposition reaction has been studied include dialkyl thiocarbonates (ROC(O)SR'),[6] aralkyl carbonates (ROC(O)OAr),[7] and dialkyl carboxylic carbonic anhydrides (RC(O)OC(O)OR').[8] These systems give dialkyl sulfides (RSR'), aralkyl ethers (ROAr) and alkyl esters (RC(O)OR'), respectively. The mechanisms which are proposed are completely analagous to those shown above for alkyl chloroformates and chlorosulfonylurethanes.

CHAPTER II

THE THERMAL DECOMPOSITION OF ALKOXYCARBONYL THIOCYANATES AND ISOTHIOCYANATES[9]

INTRODUCTION

The vapor phase decomposition of alkoxycarbonyl isothiocyanates, ROC(O)NCS (1), and alkoxycarbonyl thiocyanates, ROC(O)SCN (2), over glass wool at temperatures between 240° and 375° C has been investigated. The results of this investigation are herein presented.

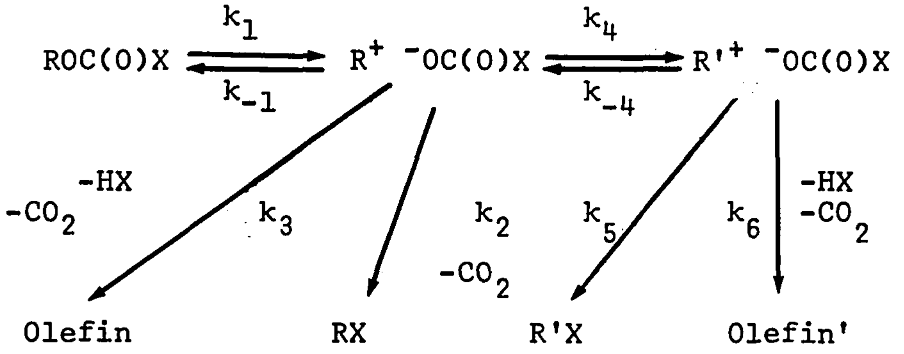
Materials (1) and (2) can be considered as compounds of the general type ROC(O)X. Others of this type have been decomposed thermally both in the liquid and vapor phase yielding RX and carbon dioxide. Investigations in which X = Cl[3,10], SR[6], OAr[7], OC(O)R[8] and $NHS(O)_2Cl$[5] have been reported.

Although the pyrolysis conditions varied substantially in the various reports, all the previous studies resulted in proposals that the decompositions occur *via* ion pair intermediates. The various side reactions (predominantly elimination and Wagner-Meerwein rearrangements) which were observed in these studies were rationalized in terms of the degree of dissociation of the ion pair, as well as the basicity of X. For example, when alkyl chloroformates

(X = Cl) were decomposed in the vapor phase at reduced pressure, the reaction proceeded with complete retention of configuration.[3] Furthermore, no alkyl shifts were observed and the amount of olefin which was produced was small. These data have been interpreted in terms of an intimate ion pair intermediate. However, when the decomposition was accomplished *via* gas chromatography, substantial amounts of elimination and rearrangement products were obtained,[4] presumably because of a greater degree of dissociation in the transition state.

A generalized mechanism consistent with the results of all of the above studies is given in Figure I.

Figure I:
Generalized Scheme for Thermal Decomposition of ROC(O)X

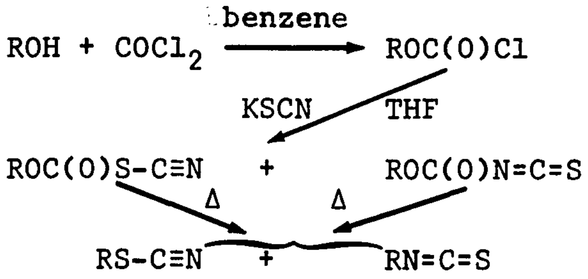


When X = -S-C≡N(-N=C=S), the decarboxylation reaction can, in principle, yield both an alkyl thiocyanate, R-S-C≡N (3), and an alkyl isothiocyanate, R-N=C=S (4). If the decarboxylation reaction shows some selectivity for one of the isomers, then this may provide a convenient method for the conversion of an alcohol into either a thiol or an amine, since these are readily obtainable from the alkyl thiocyanate and alkyl isothiocyanate respectively. Results of the decarboxylation reaction and the viability of using the aforementioned route to obtain thiols or amines from alcohols are discussed below.

RESULTS AND DISCUSSION

A. General Synthesis: All the reported syntheses of alkoxycarbonyl thiocyanates and isothiocyanates involve reaction of a thiocyanate salt (e.g., Pb^{++}, NH_4^+, K^+) with an alkyl chloroformate. The latter are obtainable (usually in high yield) by treatment of an alcohol with phosgene.[11] We prefer a modified version of the method reported by Takamizawa *et al*.[12] This involves the slow addition of an alkyl chloroformate to a heterogeneous mixture of anhydrous potassium thiocyanate in dry tetrahydrofuran under a nitrogen blanket. One obtains from this reaction a mixture of the alkoxycarbonyl thiocyanate and isothiocyanate in 45-80% yield. If one uses equal molar amounts of potassium thiocyanate and alkyl chloroformate, one obtains approximately equal amounts of both isomers; if a large excess of potassium thiocyanate is used, the alkoxycarbonyl isothiocyanate is obtained almost exclusively.[13] Both isomers undergo thermal decarboxylation to yield a mixture of alkyl thiocyanates, RS-C≡N, and alkyl isothiocyanates, RN=C=S. The overall synthesis is given in Figure II.

Figure II: Synthesis and Decomposition Scheme for ROC(O)S-C≡N and ROC(O)N=C=S



B. Pyrolysis Results: In choosing a system which will efficiently effect the decarboxylation of (1) and (2), three factors must be taken into consideration: (i) the effect of pressure, (ii) the contact time (i.e., the time in which the material is in direct contact with the hot surface), and (iii) the sometimes facile isomerization of alkyl thiocyanates to alkyl isothiocyanates.

The effect of pressure on the decompositions of both (1) and (2) is found to be quite significant. For example, if these decompositions are studied *via* gas liquid chromatography (glc),[14] only very small amounts (0.5-3.0%) of the expected alkyl thiocyanate and isothiocyanate are obtained. The major product is polymer, although small amounts of dialkyl carbonates, $(RO)_2CO$, are also isolated. Since these dialkyl carbonates must be the product of, at least, a bimolecular process, observation of these products in "low pressure" pyrolyses over glass wool constitutes an indication that either the pressure is too high or that the rate of addition to the hot surface is too rapid.

When the decompositions are performed at reduced pressure significantly higher yields of alkyl thiocyanates and isothiocyanates are obtained. The highest yields of these products were obtained when (1) or (2) had prolonged contact with a hot surface at reduced pressure.

The method found to effect these decompositions most efficiently is to allow the vaporized (1) or (2) to pass through a 100 cm. column packed with glass wool at a pressure of 5 Torr. A diagram of the complete pyrolysis apparatus is given in Fig. III. The material is vaporized by dripping it on a hot connecting joint. The pressure drop across the glass wool causes the material to flow through the column (the contact time is three to four minutes). The pyrolysate is collected in a cold trap at -78° C. Thus, this system has the dual advantage of allowing relatively long contact times, while at the same time minimizing the possibility of the decarboxylated product undergoing further reaction because of continued contact with the hot surface as in glc decompositions.

The results of the pyrolysis of five alkoxycarbonyl isothiocyanates and four alkoxycarbonyl thiocyanates are given in Table I. The temperature at which the pyrolysis is listed as being performed is that temperature at which the maximum yield of either alkyl thiocyanate or alkyl isothiocyanate was obtained. For example, when (1b) was pyrolyzed under reaction conditions identical to those in Table I at 325° C, a 50% yield of (3b) was obtained. The remainder was unreacted (1b) and trace amounts of (4b). When (1b) was pyrolyzed at 375° C, (3b) was produced in 25% yield and (4b) in 50% yield. When (1b) was pyrolyzed at 350°, a 90% yield of (3b) was obtained.

From the pyrolysis temperatures given in Table I, it is apparent that as more alkyl substituents are added to the carbinolic carbon, a decrease in the temperature at which alkyl thiocyanates or isothiocyanates are produced most efficiently is observed. Furthermore, the fact that in all cases isomers (1) and (2) decompose to give essentially the same product ratios suggests a common intermediate. While these results taken alone do not unequivocally indicate a particular reaction pathway, their consistency with the generalized mechanism for other ROC(O)X systems (Figure I) is apparent.

From the results in Table I it is also seen that (1a), (1b), (2a), and (2b) yield predominantly S-substituted products, (1c), (1e) and (2c) predominantly N-substituted products, and (1d) and (2d) a mixture of N- and S- substituted products. These data can be explained in terms of an initial formation of S-substituted product, followed, in some cases, by isomerization.[16] This explanation was verified by the performance of a number of pyrolyses at lower than optimum temperatures. For example, when (1c) was pyrolyzed at 230° C. under typical experimental conditions a 5% conversion to (3c) could be detected in the nmr spectrum of the pyrolysate; no (4c) was observed. At 270° C., the pyrolysate was composed of (3c) (16%), (4c) (30%) and (1c) (54%). Thus, it appears that (3c) is formed initially, but isomerizes readily to (4c). In general, only simple primary thiocyanates were slow to isomerize under the experimental conditions.

Synthetically, the viability of using the pyrolysis of primary alkoxycarbonyl thiocyanates and isothiocyanates as a general method for the synthesis of primary alkyl thiocyanates is of questionable value. Although the overall process gives product in good yield, similar results can be obtained by less tedious methods.[17] However, this method does appear to be potentially important for the syntheses of secondary and tertiary alkyl isothiocyanates,[18] not only because of the high overall yield, but also because of the lack of rearrangement and elimination products.[19]

Furthermore, since alkyl isothiocyanates can be hydrolyzed to the corresponding amine[20] or reduced (catalytically or with lithium aluminum hydride) to the corresponding methyl amines in high yield,[21] this process can be extended to provide a general method for the conversion of a secondary or tertiary alcohol to the corresponding amine (or methyl amine) in 25-55% overall yield from the alcohol, based upon normal yields in these reactions.

EXPERIMENTAL SECTION

Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, New York. Nmr spectra were measured on a Varian A-60A spectrometer in CCl_4 solution using tetramethylsilane as an internal standard unless otherwise noted. Mass spectra were measured on a Varian MAT CH-7 spectrometer at 70 ev. Infrared spectra were measured on a Perkin-Elmer 237-B spectrophotometer. Phosgene (12.5% solution in benzene) was purchased from Matheson, Coleman and Bell, Inc., and used without further purification. Tetrahydrofuran was dried over sodium ribbon and distilled prior to use. The potassium thiocyanate was dried either by fusing it and allowed it to cool in a dessicator or by allowing it to stir for four hours in 2,2-dimethoxyethane, folllowed by filtration and thorough washing with dry tetrahydrofuran.

General Synthesis of Alkyl Chloroformates: A molar equivalent of the appropriate alcohol dissolved in benzene was added slowly to a two-fold excess of phosgene in benzene at room temperature under nitrogen atmosphere. The solution was stirred for three hours after which the benzene and excess phosgene were removed by distillation at reduced pressure. All chloroformates were used without further purification.

General Synthesis of Alkoxycarbonyl Thiocyanates and Iso-Thiocyanates: A solution of the appropriate alkyl chloroformate in dry tetrahydrofuran was added slowly to a suspension of anhydrous potassium thiocyanate in dry tetrahydrofuran under nitrogen atmosphere with vigorous stirring. If a molar equivalent of potassium thiocyante was used, an approximately equal mixture of the alkoxycarbonyl thiocyanate and isothiocyanate was obtained; if excess potassium thiocyanate was used, only the alkoxycarbonyl isothiocyanate was obtained. Both isomers were capable of being isolated in the pure state by distillation using a good fractionating column (Vigreux) or a teflon spinning-band at low pressure.

Pyrolysis Procedure: A 100 cm Pyrex tube was packed tightly with Pyrex glass wool. The pyrolysis apparatus was assembled as shown in Figure I and given at least one hour to reach thermal equilibrium. The pyrolysis temperature was measured by means of a thermocouple at the center of the oven. The heated connecting joint was made by winding a Nichrome wire around a suitably shaped piece of Pyrex glass, insulating it with asbestos paper, and regulating it with a variable transformer. During pyrolyses, this region was normally maintained at 250° C.

Although the pressure was maintained at 5 Torr in all cases reported here, no significant differences were noted with small variations in the pressure (± 2 Torr). In general, it was found that approximately 10 gm of material could be pyrolyzed in a period of one hour. Faster rates of addition usually resulted in the formation of small amounts (ca 5%) of products resulting from bimolecular reactions.

Pyrolysis Results: The product mixtures were analyzed by gas-liquid-chromatography (glc) using a 5' x 1/4" column of Apiezon L on Chromsorb W at temperatures of 100-150° (flow rate of He = 200 ml/min) or more conveniently with nmr by measurement of the relative signal intensities of the protons adjacent to the -SCN or -NCS groups.[22] The products were purified by distillation, with the exception of (4e) which was recrystallized from a 1:1 mixture of benzene/petroleum ether. The identities of the materials were determined by comparison of their physical and spectral properties with those of authentic materials which were synthesized independently.

Independent Synthesis of Alkyl Thiocyanates and Isothiocyanates: Alkyl thiocyanates and isothiocyanates were prepared from the corresponding alcohols *via* the tosylates. The tosylates were prepared by the general method given by Fieser,[24] summarized as follows: 10 gm of the appropriate alcohol were added to one molar excess of para-toluenesulfonyl chloride in 125 ml of dry pyridine at 0°. The reaction was placed in the refrigerator for 24 hr, by which time meedles of pyridine hydrochloride had precipitated from solution. The mixture was poured onto 600 gm of ice and then extracted three times with ether. The ethereal solution was washed twice with 6 M HCl and then with water. The solution was dried over K_2CO_3-Na_2SO_4 and the ether evaporated at room temperature at reduced pressure.

The resulting oil was dissolved in acetone and added dropwise to a solution of potassium thiocyanate dissolved in acetone. The reaction was allowed to stir for 2-6 hr after which it was filtered. The acetone was removed by distillation at reduced pressure and the remaining liquid (which sometimes needs further filtration) was distilled at the appropriate temperatures given in Table III. While the relative amounts of alkyl thiocyanate and isothiocyanate produced varied, significant quantities of both isomers could always be obtained.

The only compound not independently synthesized was (4e) which was commercially available from Aldrich Chemical Co., Inc.

TABLE I

	Reactant	Temp., 5 Torr		% Thiocyanate[a]		% Isothiocyanate[a]
1a	$CH_3OC(O)NCS$	360°	3a	CH_3SCN (81%)	4a	CH_3NCS (4%)
2a	$CH_3OC(O)SCN$	360°	3a	CH_3SCN (78%)	4a	CH_3NCS (3%)
1b	$C_2H_5OC(O)NCS$	350°	3b	C_2H_5SCN (90%)	4b	C_2H_5NCS (5%)
2b	$C_2H_5OC(O)SCN$	350°	3b	C_2H_5SCN (90%)	4b	C_2H_5NCS (2%)
1c	$(CH_3)_2CHOC(O)NCS$	300°	3c	$(CH_3)_2CHSCN$ (6%)	4c	$(CH_3)_2CHNCS$ (84%)
2c	$(CH_3)_2CHOC(O)SCN$	300°	3c	$(CH_3)_2CHSCN$ (3%)	4c	$(CH_3)_2CHNCS$ (84%)
1d	$(CH_3)_2CHCH_2OC(O)NCS$	335°	3d	$(CH_3)_2CHCH_2SCN$ (32%)	4d	$(CH_3)_2CHCH_2NCS$ (60%)
2d	$(CH_3)_2CHCH_2OC(O)SCN$	335°	3d	$(CH_3)_2CHCH_2SCN$ (30%)	4d	$(CH_3)_2CHCH_2NCS$ (63%)
1e	1 - AdOC(O)NCS[b]	275°	3e	AdSCN[c] (0%)	4e	AdNCS (88%)

a) These isolated yields are given as percentage of the theoretical yield. No rearrangement of the alkyl groups was observed.

b) Ad = adamantyl

c) No adamantyl thiocyanate was isolated.

a) Satisfactory analytical data were reported for all new compounds listed in the table, with the exception of (1d) and (2d). These compounds gave analyses which were approximately 1.1% and 0.6% from the calculated % C and % H, respectively. Although these compounds distill as clear, colorless liquids, they begin to yellow within 15 minutes after distillation even in a nitrogen atomosphere in the dark. While the nmr spectra of these compounds, taken immediately after distillation, indicate no detectable impurities, spectra of material which has been allowed to stand for 30 minutes shows a small, but definite broadening in the peak widths. These results indicate that a small amount of decomposition occurs even under relatively innocuous conditions, and thus tend to make good analytical data unobtainable unless combustion analyses are performed immediately after distillation.

b) Since isomers (1) and (2) yield the same products upon pyrolysis, mixtures of the two can be used for synthetic purposes. This is most convenient as separation of (1) and (2) is no longer necessary. Thus, the % yield of usable material is actually the sum of the yield of (1) and (2).

c) These absorptions are weak. All other ir absorptions listed are strong.

d) 115 represents (M^+ - 44). No M^+ is observed. Apparently the molecular ion undergoes facile decarboxylation.

TABLE II

Cmpd.[a]	% Yield[b]	Mp or bp, °C (Torr)	Ir, μ	Nmr, δ	Ms
1a	20	29-33 (3.0)	5.08, 5.70	3.73 (s)	117
2a	25	42-45 (3.5)	4.59,[c] 5.60	4.18 (s)	117
1b	26	26-27 (1.7)	5.10, 5.72	4.15(q,2),1.23(t,3)	131
2b	35	40-42 (2.0)	4.62,[c] 5.60	3.70(q,2),1.21(t,3)	131
1c	28	40-42 (0.8)	5.05, 5.72	4.94(m,1),1.37(d,6)	145
2c	38	53-54 (0.6)	4.60,[c] 5.61	5.20(m,1),1.38(d,6)	145
1d	26	35-38 (0.3)	5.07, 5.72	4.50(d,2),2.30(m,1),1.20(d,6)	115[d]
2d	46	49-54 (0.3)	4.60,[c] 5.61	4.27(d,2),2.27(m,1),1.20(d,6)	115[d]
1e	80	121-122	5.05, 5.75	1.57(s,9),2.11(s,6)	237

TABLE III

Cmpd.[23]	Bp(mp) °C	Ir, μ (-SCN or -NCS)	Nmr, δ
3a	133-134	4.61 (sh)	2.61(s)
4a	117-119 (35)	4.73 (b)	3.57(s)
3b	146-148	4.62 (sh)	2.98(q,2), 1.50(t,3)
4b	131-132	4.79 (b)	3.64(q,2), 1.15(t,3)
3c	152-154	4.65 (sh)	3.48(m,1), 1.49(d,2)
4c	137-138	4.82 (b)	3.95(m,1), 1.31(d,2)
3d	175-176	4.62 (sh)	2.92(d,2), 1.95(m,1), 0.97(d,2)
4d	161-163	4.78 (b)	3.33(d,2), 1.71(m,1), 1.08(d,2)
4e	(167-168)	4.70, 4.78, 4.86 (b)	2.10(s,9), 1.68(s,6)

sh = sharp; b = broad

FIGURE III

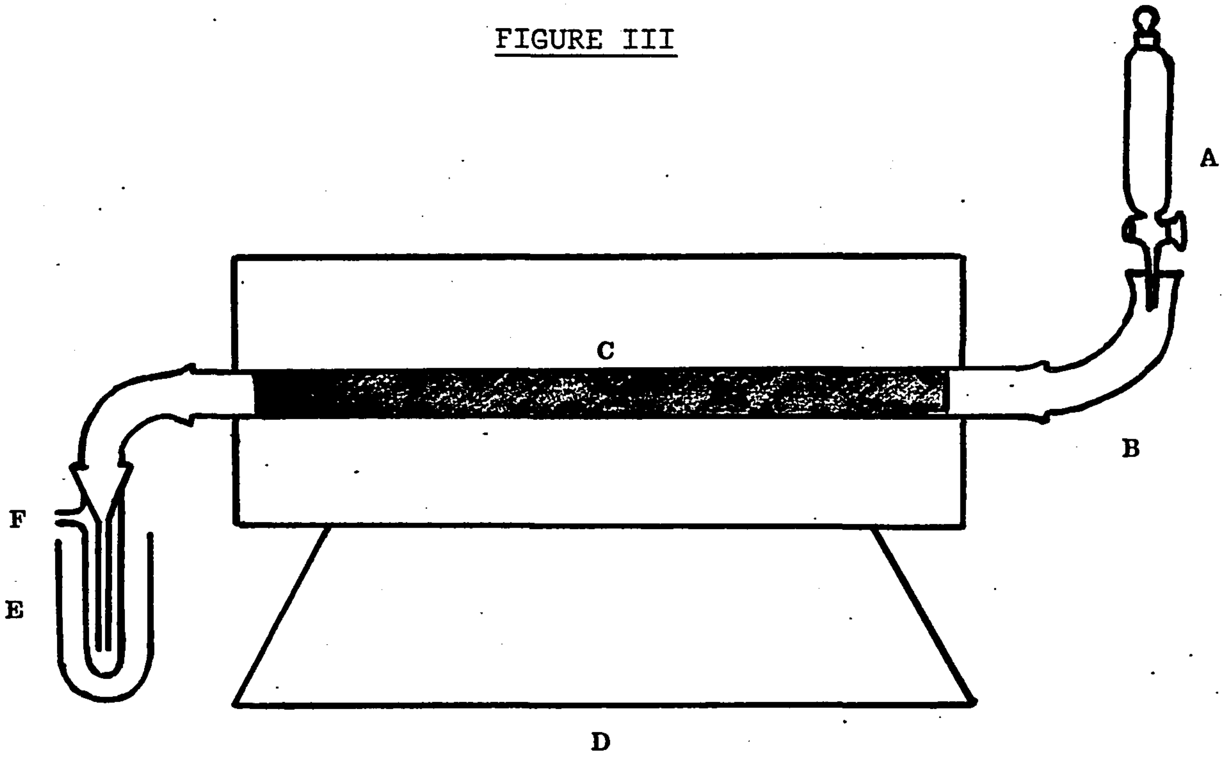


FIGURE III CAPTIONS

A - 60 ml addition funnel

B - heated connecting joint

C - 100 cm Pyrex column packed with 65 g glass wool over a length of 85 cm

D - Lindberg Hevi-Duty Combustion Furnace, Model No. 59744

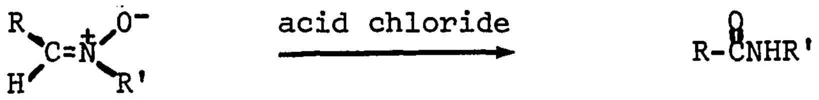
E - dry ice/isopropanol cold trap

F - outlet to vacuum pump and point at which pressure is measured

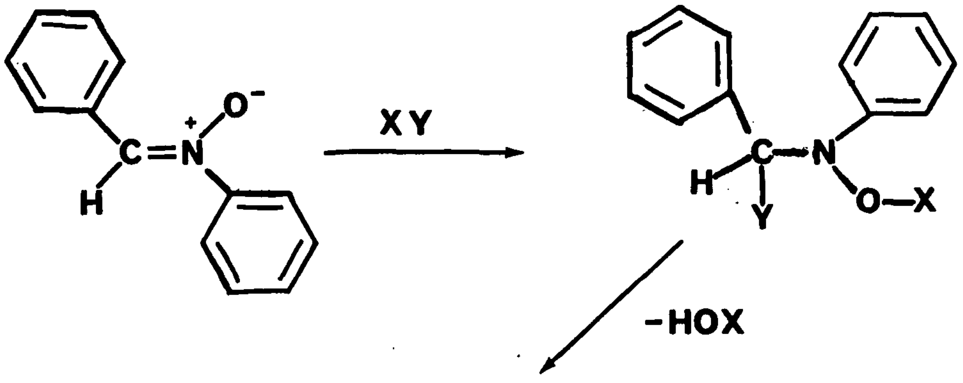
CHAPTER III

ACID CHLORIDE CATALYZED ISOMERIZATIONS OF ALDONITRONES TO AMIDES

Aldonitrones are reported to isomerize to the corresponding amides by treatment with a wide variety of reagents. These include, inter alia, acetyl chloride, acetic anhydride, phosphorous pentachloride, phosphorous oxychloride, benzoyl chloride and sulfur dioxide.[25]



Kroehnke proposed that this process occurs via an addition-elimination on the C,N double bond, as shown below for α,N-diphenyl nitrone (R=R'=phenyl) and acetic anhydride (X=Ac, Y=OAc):



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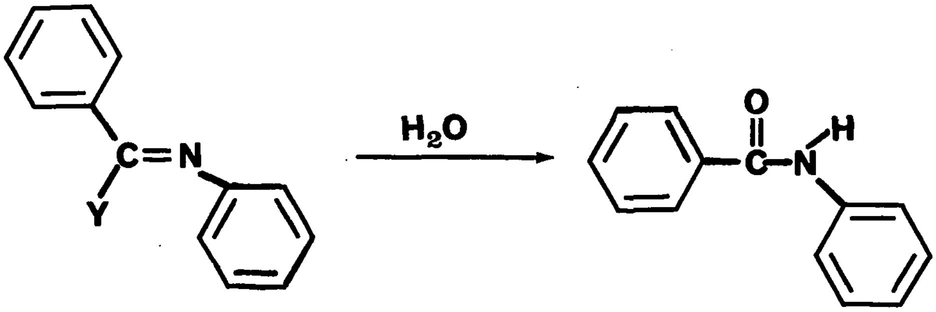
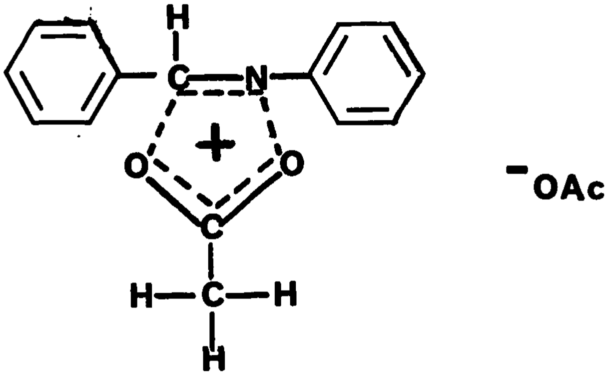


In a later study Umezawa[27] suggested that these reactions proceed via the cyclic intermediate which is shown below:

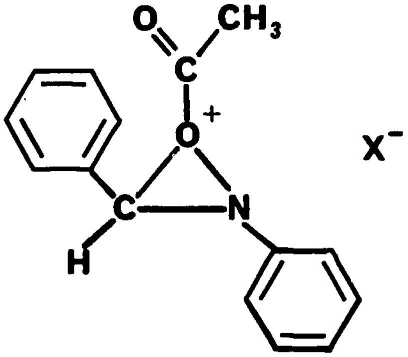


This intermediate can then lose acetic acid to form the same acetoxy imine proposed by Kroehnke. However, contrary to Kroehnke's mechanism, Umezawa proposed that this acetoxy imine reacts with acetic acid to form the amide and regenerate acetic anhydride.

That this reaction is indeed an intramolecular process was claimed on the basis of results of an ^{18}O-labelling study performed by Oae *et al*.[28] In it they found that the amount of ^{18}O incorporated into the amide was constant, irrespective of the molar ratio of labelled acetic anhydride to diphenyl nitrone which was used. Furthermore, the large acceleration in the reaction rate observed for strong electron-releasing groups (*e.g.*, *para*-CH_3O- and *para*-$(CH_3)_2N$-) attached to the α-phenyl ring, correlates well with the intermediate proposed by Umezawa.

In the same study Oae *et al*. succeeded in isolating the acetoxy imine discussed above. Its structure was elucidated by ir, nmr, ms and combustion analysis. This compound gave the amide when exposed to moisture, but was stable to acetic acid.

An interesting alternative to the mechanism discussed above was proposed by Lamchen.[29] He suggested the possibility that the reaction could proceed via an acylated oxaziridine intermediate, which is shown below:



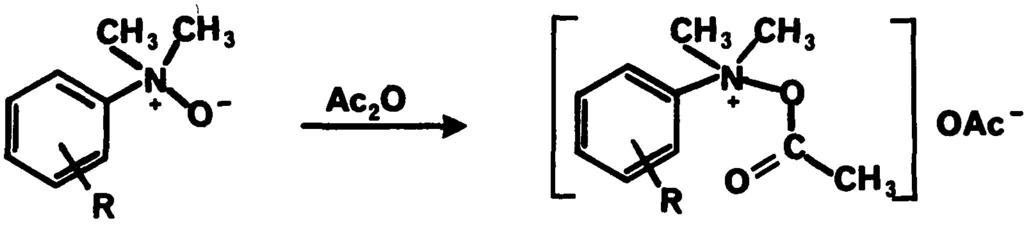
While this mechanism is applicable to all the acid chlorides and anhydrides mentioned earlier, ^{18}O-labelled acid chlorides and anhydrides would be expected to show no incorporation of the label in the resulting amide. However, in cases in which ^{18}O- incorporation is incomplete, this mechanism cannot be ruled out as a competing pathway.

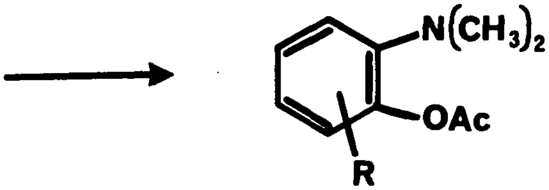
CHAPTER IV

SELECTIVE ORTHO-CHLORINATION IN THE REACTIONS OF ARYL NITRONES AND AMINE OXIDES WITH THIONYL CHLORIDE OR PHOSGENE

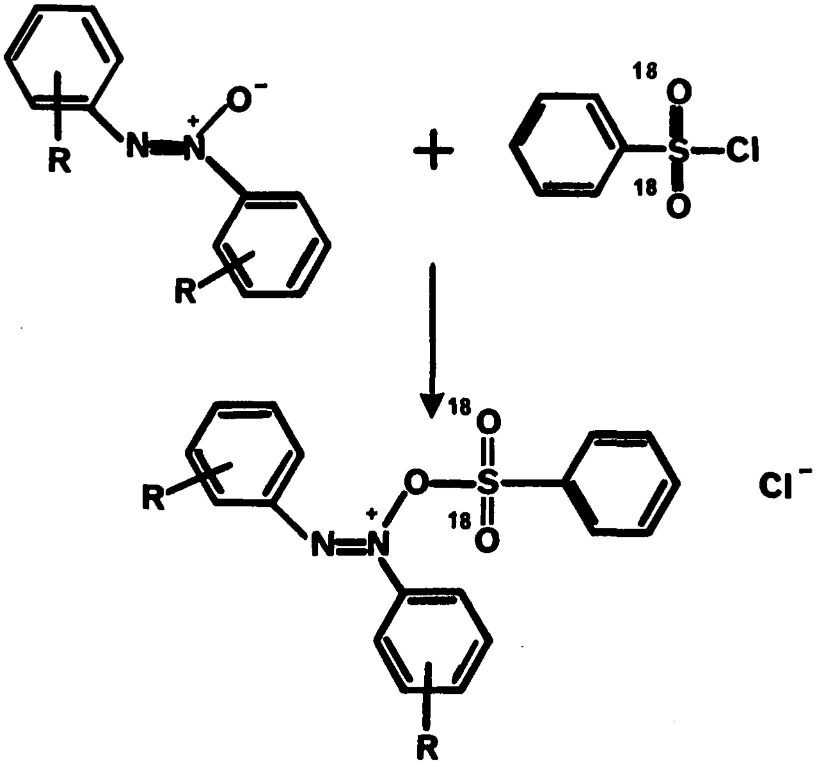
INTRODUCTION

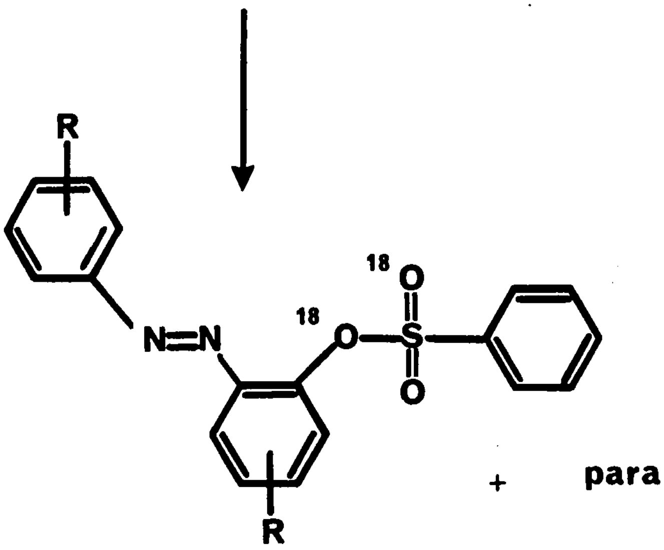
The classes of N-aryl nitrogen oxides which are of current interest in this laboratory include, inter alia, N-arylnitrones, N-aryl tertiary amine-N-oxides, N,N'-diarylazoxy compounds, nitroaromatic compounds, and N-aryl-N-nitroso dimers. A few of the above have been reported to react with acid chlorides and anhydrides to yield ring substituted products. For example, in an investigation of the Polonovski reaction, Huisgen, et al.[30] have obseved the production of small to moderate amounts of ortho-acetylated N,N-dimethylanilines when ring substituted N,N-dimethylaniline-N-oxides were allowed to react with acetic anhydride. The reaction was thought to proceed through an N-acetoxy-N,N-dimethylanilinium acetate as shown below:





Similarly, although N,N'-diarylazoxy compounds undergo deoxygenation when treated with most acid chlorides,[31] they yield <u>ortho</u>- and <u>para</u>-ring substituted products when allowed to react with benzenesulfonyl chloride.[32] The <u>ortho</u>-substituted product has been shown by ^{18}O isotope labeling to be formed from an intermediate similar to the one proposed by Huisgen for the amine oxide reaction.





N-Aryl nitrones are reported to isomerize to the corresponding amides when allowed to react with most acid chlorides and anhydrides.[25] However, in a preliminary communication from this laboratory, it was recently reported that N-aryl nitrones react rapidly with thionyl chloride or phosgene at room temperature to yield the corresponding ortho-chlorinated imine hydrochlorides in high yield.[33] The remarkable positional selectivity of this reaction prompted us to investigate the mechanism by which it occurs and to test its generality with other N-aryl nitrogen oxides and analagous systems. We now report the results of our investigation.

RESULTS AND DISCUSSION

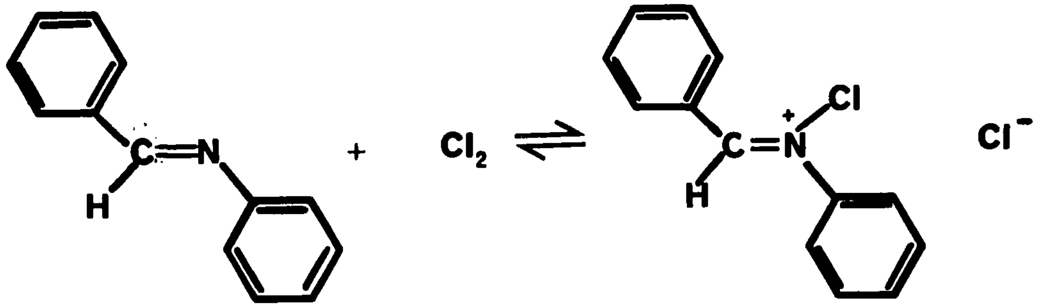
A. Nitrones: In general, the reactions are performed as follows: the aryl nitrone is dissolved at room temperature in dry benzene and thionyl chloride (or phosgene dissolved in benzene) is added dropwise. The evolution of a gas and simultaneous production of a precipitate occur almost immediately. After the addition is completed the precipitate is collected and washed with pentane. Although this procedure is usually sufficient to obtain a reasonably pure product, further purification can be accomplished by vacuum sublimation. The results are summarized in Table IV.

Since aryl nitrones are readily available by several methods,[34,35] the above reaction appears generally useful for the selective, rapid, synthesis of ortho-chlorinated imines, and by hydrolysis, the corresponding amines in high yield.

While several pathways might be proposed for this reaction, only one is reasonable in light of the evidence at hand. This is illustrated in Figure IV for the reaction of α,N-diphenylnitrone (5) with phosgene.

The first step of the reaction undoubtedly involves nucleophilic attack on the phosgene by the negatively charged oxygen atom of the nitrone yielding Intermediate I. An appropriately positioned nitro group would therefore be expected to decrease the rate of reaction by delocalization of the negative charge, and, in fact, α-4-nitrophenyl-Nphenylnitrone (11) is the only nitrone among those investigated which requires heating for the reaction to occur. The Intermediate I may be viewed as decomposing to products via a concerted decarboxylation with ring chlorination followed by hydrogen transfer with rearomatization.

The positional selectivity of the reaction rules out two other possible mechanisms which might have been worthy of consideration. For the first of these, Intermediate I would be considered to rearrange to an N-chloroimmonium species (Intermediate II) followed by ring substitution. As Intermediate II is an expected constituent of an equilibrium mixture of (22) and chlorine,[36] generation of this species by addition of a dilute solution of chlorine in benzene to the anil (22) is possible. In fact, when this experiment was performed, a precipitate formed immediately, analysis of which indicated it to be an equal mixture of benzylidene aniline hydrochloride and benzylidene para-chloroaniline hydrochloride;[37] no ortho- isomer was detected.



(22) Intermediate II

This result precludes the possibility of the reaction proceeding through Intermediate II.[38] Another alternative mechanism, that of chloride attack on the N-aryl ring of Intermediate I, is excluded as well as that route would be expected to yield a significant proportion of para- product.

The extremely high ortho:para ratio observed in all reactions is indeed significant evidence for the reaction to be considered as proceeding through a six-centered transition state. Comparison with other ring halogenation processes involving N-chloro intermediates is illustrative of this point. Whereas, for example, N-chloro-N-methylaniline is reported to rearrange to ring chlorinated products with an ortho:para ratio of approximately 2:1,[39] the products of these nitrone reactions had ortho; para ratios ranging from a minimum value of about 13.5 : 1 to those cases where no para isomer could be detected.[40] Thus, we consider the reaction to proceed via the six-centered transition state and therefore to be analagous to the reactions reported by Huisgen, et al.[30] and by Oae et al.[33] (vide supra). In view of this it is not surprising that in all the nitrone reactions studied chlorination was only obseved on the N-aryl ring even when the C-aryl ring contained substitutents highly activating for electrophilic substitution, e.g.(18)

B. Amine Oxides: Since thionyl chloride and phosgene react with N-aryl nitrones so selectively, it was of interest to determine if other N-aryl nitrogen oxides would react in a similar fashion. To this end, N,N-dimethylaniline-N-oxide (23), prepared from N,N-dimethylaniline (24) and hydrogen peroxide in aqueous methanol,[41] were allowed to react with thionyl chloride. Because of the hygroscopic nature of (23), the reaction was performed in a glove bag in a nitrogen atmosphere. Various solvents were used (benzene, chloroform, tetrahydrofuran, petroleum ether). The major competing process with ring chlorination proved to be deoxygenation of the amine oxide to (24). This latter reaction could be minimized by working with dilute solutions of the amine oxide in petroleum ether or tetrahydrofuran, in which case approximately 90% N,N-dimethyl-2-chloroaniline (25) was obtained. This compares with 30% (25) and 70% (24) being obtained when the reaction was performed in more concentrated solutions.

Although reaction conditions can be optimized to give good yields of ring chlorinated product, the reaction is restricted to tertiary amine systems, and hence, is less versatile than the ortho-chlorination of nitrones. Nevertheless, as this reaction appears to be basically similar to that of nitrones, it is obvious that a pi-bonded nitrogen is not required.

C. Other Systems: Other N-aryl oxides which might be expected to react with thionyl chloride or phosgene in a similar fashion to nitrones or amine oxides apparently do not.

Nitroaromatic compounds appear to react very slowly with thionyl chloride. A small amount of reaction appears to occur upon setting to reflux for one week a mixture of nitrobenzene (26) with thionyl chloride, as the solution becomes distinctly purple in color. Nevertheless, it has been proven impossible to identify any organic compounds other than (26) in the reaction mixture.

The reaction of N,N'-diaryl azoxy compounds with a number of acid chlorides including thionyl chloride has been previously investigated.[31] We confirmed that deoxygenation appears to be the major process, with ring chlorination as a minor competing side reaction.

Nitroso compounds exist in the dimeric N-oxide form only in the solid state. We have shown in this laboratory that reaction does occur between nitrosobenzene (27) and thionyl chloride, but along different lines from the amine oxides and nitrone reactions. The major product is 2,4-dichloroaniline (28), presumably arising from rearrangement of N,N-dichloroaniline.[42] Iodosobenzene (29) when treated with thionyl chloride yields iodobenzene dichloride (30) quantitatively.[43]

EXPERIMENTAL

General: All melting points were measured using a Thomas-Hoover Capillary Melting Point Apparatus and are uncorrected.

Unless otherwise stated, infrared spectra were measured as Nujol or Fluorolube mulls on a Perkin-Elmer 237-B grating spectrometer; mass spectra were measured using a Varian CH-7 mass spectrometer; NMR spectra were measured using either a Varian A60-A or Varian EM-360 spectrometer. Benzene and tetrahydrofuran were dried over sodium ribbon and distilled prior to use. Phosgene (12.5% solution in benzene) and thionyl chloride were purchased from Matheson, Coleman, and Bell and used without further purification.

Nitrones: All nitrones were prepared according to the standard procedure as follows:[44] equal molar quantities of the aryl hydroxylamine and the aldehyde were mixed in benzene solution and refluxed, water being removed in a Dean-Stark apparatus. In general, these reactions went to completion in a very short time. The solvent was evaporated and the crude nitrone recrystallized from a 1:1 mixture of low boiling petroleum ether and benzene. All of the nitrones utilized in this investigation have been reported in the literature[44,45] with the exception of (20). This was isolated in 80% yield (m.p. 141-142°) by the above procedure. Compound (20) exhibited a mass spectrum in accord with the nitrone structure,[46] (M^+, m/e = 269; base peak, $[M-28]^+$, m/e = 241); other analytical data are as follows: ir ($CHCl_3$) 3.32, 5.78, 6.14, 6.84, 6.95, 7.09, 7.22, 7.75, 8.13, 8.33, 8.48, 8.93, 9.09, 9.18, 9.71, 11.11, 11.37, 14.39. 14.82 μ; nmr ($CDCl_3$) δ 1.40 (t,3H), 4.38 (q,2H), 7.2-8.5 (m,10H); Anal., calcd. for $C_6H_{15}NO_3$, C: 71.37%, H: 5.58%; Found, C: 71.62%, H: 5.86%[47]

<u>General Procedure for the Reaction of Nitrones with Thionyl Chloride (or Phosgene)</u>: The aryl nitrone was dissolved in benzene and to it was added thionyl chloride (phosgene in benzene, 12.5%) dropwise in 10% molar excess. The precipitate which immediately formed was collected and washed with pentane. Rigorous purification was effected by vacuum sublimation. The various substituted imine hydrochlorides were compared with authentic materials synthesized by a standard independent means from the appropriate amines and aldehydes *via* azeotropic distillation using a Dean-Stark apparatus.[48] The isolated imines were dissolved in benzene and treated with anhydrous HCl to yield the imine hydrochlorides necessary for product comparison. There appears to be no prior report of compound (21) or its corresponding imine, thus special analysis was done in this case (*vide infra*). Product authentication in the other cases was done by mixed melting point and comparison of ir, and mass spectral data. This data is listed for convenience in Table V (A and B). To firmly establish the structure of (21) a degradative study was performed. It was first treated with 1:1 10% hydrochloric acid/tetrahydrofuran, the resulting benzaldehyde being extracted into ether, and identified through ir

spectrometry and by preparation of its 2,4-dinitrophenylhydrazone. The resulting aqueous layer was brought to alkaline pH and extracted with ether. Evaporation of the ether yielded 4-amino-3-chlorobenzoic acid ethyl ester (31). Compound (31) was then further hydrolyzed with 40% aqueous sodium hydroxide solution at reflux temperature for fifteen minutes. The solution was allowed to cool and the pH was adjusted to 4.5. The 4-amino-3-chlorobenzoic acid (32) which precipitated was recrystallized from 85% aqueous tetrahydrofuran, m.p. 222-224°.[49] Mass spectral and ir data for (21) are given in Table V (B). Anal. for (21), calc. for $C_{16}H_{15}NO_2Cl_2$, C: 59.26%, H: 4.63%; Found, C: 59.39%, H: 4.88%.

General Procedure for the Reaction of N,N-Dimethylaniline N-Oxide with Thionyl Chloride: Compound (23) was prepared according to a method described previously.[41] It was dried through azeotropic distillation with benzene, then filtered in a nitrogen atmosphere in a glove bag. A 10% molar excess of thionyl chloride was then added dropwise to a solution of (23) in various solvents (chloroform, tetrahydrofuran, benzene and petroleum ether were tried in different runs). After the addition was complete, the solution was made basic with aqueous sodium hydroxide and the organic fraction was collected, dried ($MgSO_4$) and evaporated. The crude products obtained in each run were examined by gas-liquid chromatography (30% Carbowax on Chromosorb P, 180°) and by mass spectrometry. Unless dilute solutions (e.g., 1%) of (23) were used, significant quantities of N,N-dimethylaniline (24) were formed along with 2-chloro-N,N-dimethylaniline (25), sym-trinitrobenzene adduct, m.p. 108.5-109° (lit 110-111°)[50]; m/e = 154,156. With dilute solutions of (23) in tetrahydrofuran or petroleum ether, (25) was obtained as the only significant product.

General Procedure for the Reaction of Nitrosobenzene (27) With Thionyl Chloride: Nitrosobenzene (27) was dissolved in benzene, and thionyl chloride was added dropwise in 10% molar excess. An immediate reaction occured. The product was isolated by bringing the reaction mixture to pH = 11, extracting with ether, drying the organic material ($MgSO_4$) and evaporating the solvent. The product was proven to be 2,4-dichloroaniline (28) by mass spectrometry, m/e = 161 (100%), 163, 91, preparation of its benzylidene derivative, m.p. 84° (lit. m.p. 84°)[51] and by comparison of its ir spectrum with one reported in the literature.[52]

Reaction of Nitrobenzene with Thionyl Chloride: Nitrobenzene (26) was refluxed with a 10% molar excess of thionyl chloride for one week. After this time the solution had a distinctly purple color. However, it proved impossible to isolate any organic material other than nitrobenzene in quantities sufficient for analysis.

Reaction of Iodosobenzene with Thionyl Chloride: The procedure is exactly the same as that used for nitrosobenzene. The product was identified by comparison with iodobenzene dichloride (30), m.p. 110-111^0, which was independently synthesized.

FIGURE IV

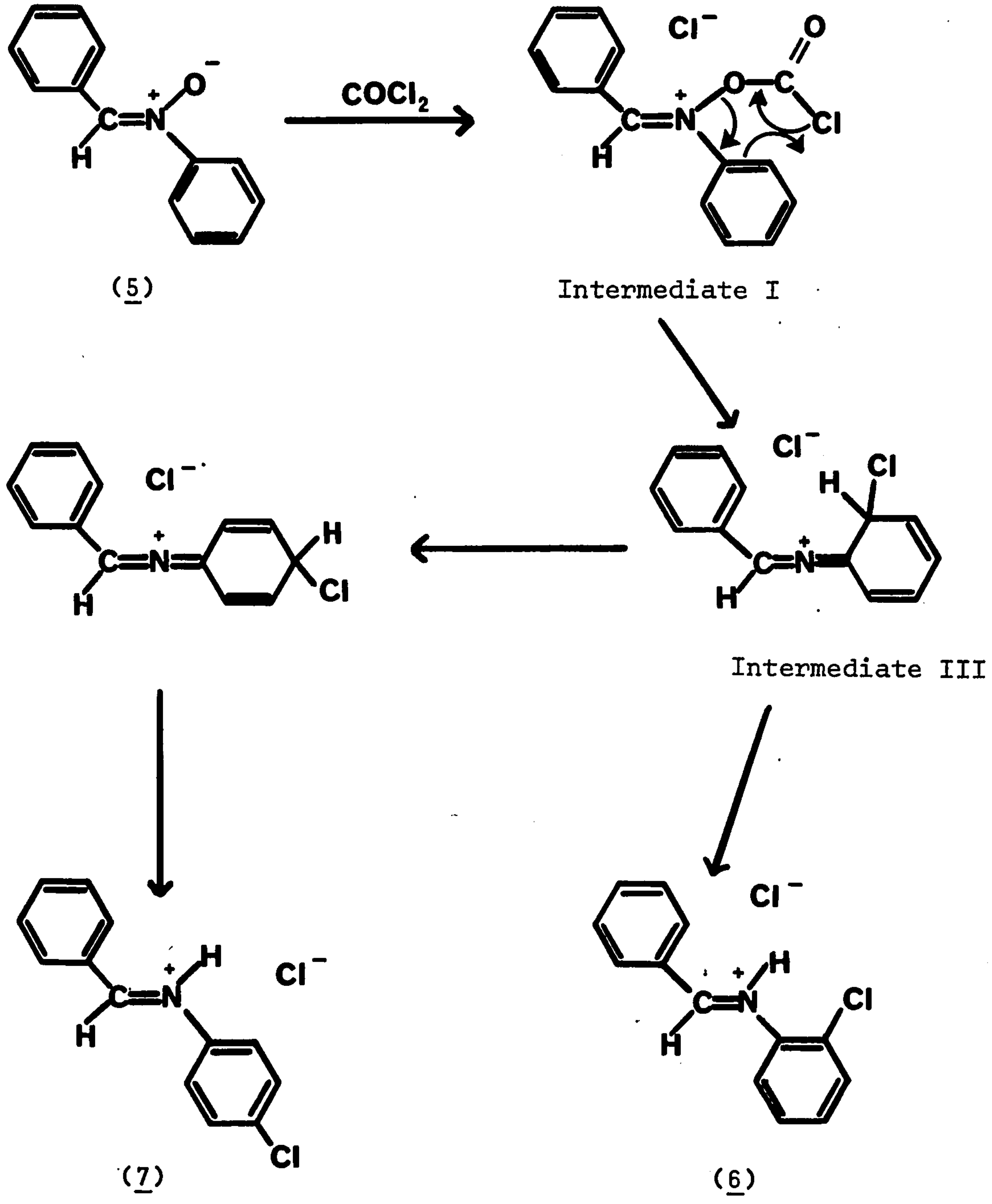
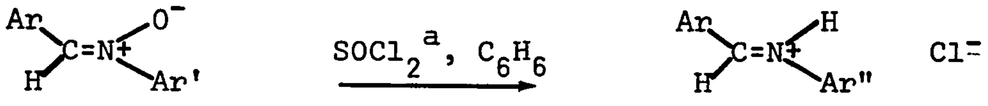


TABLE IV



Reactants			Products		
Cmpd.	Ar	Ar'	Cmpd.	Ar"	Isolated Yield (%)
5	C_6H_5	C_6H_5	6	$2\text{-}Cl\text{-}C_6H_4$	81
			7	$4\text{-}Cl\text{-}C_6H_4$	6
8	C_6H_5CHCH	C_6H_5	9	$2\text{-}Cl\text{-}C_6H_4$	72
			10	$4\text{-}Cl\text{-}C_6H_4$	3
11	$4\text{-}NO_2\text{-}C_6H_4$	C_6H_5	12	$2\text{-}Cl\text{-}C_6H_4$	83[c]
14	C_6H_5	$4\text{-}CH_3\text{-}C_6H_4$	15	$2\text{-}Cl\text{-}4\text{-}CH_3\text{-}C_6H_3$	91
16	C_6H_5	$4\text{-}Cl\text{-}C_6H_4$	17	$2,4\text{-}Cl_2\text{-}C_6H_3$	92
18	$4\text{-}CH_3O\text{-}C_6H_4$	$4\text{-}Cl\text{-}C_6H_4$	19	$2,4\text{-}Cl_2\text{-}C_6H_3$	90
20	C_6H_5	$4\text{-}H_5C_2O_2C\text{-}C_6H_4$	21	$2\text{-}Cl\text{-}4\text{-}H_5C_2O_2C\text{-}C_6H_3$[d]	94

TABLE IV

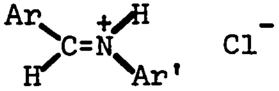
a) No significant differences in product ratios were observed when phosgene was used in place of thionyl chloride.

b) The structures of the products (except (21) were determined by comparison of their physical and spectral properties with authentic samples which were prepared independently.

c) Slight heating was necessary to initiate this reaction.

d) The structure of (21) was determined by mass spectrometry, elemental analysis, and chemical degradation to known substances.

TABLE V (A)



Compound	Ar	Ar'	M.P.
6	C_6H_5	$2\text{-Cl-}C_6H_4$	$215^{\circ}d$
7	C_6H_5	$4\text{-Cl-}C_6H_4$	$189\text{-}191^{\circ}$
9	C_6H_5CHCH	$2\text{-Cl-}C_6H_4$	$148^{\circ}d^{d}$
10	C_6H_5CHCH	$4\text{-Cl-}C_6H_4$	$167\text{-}169^{\circ d}$
12	$4\text{-}NO_2C_6H_4$	$2\text{-Cl-}C_6H_4$	$188\text{-}190^{\circ}d$
15	C_6H_5	$2\text{-Cl-}4\text{-}CH_3\text{-}C_6H_3$	$194\text{-}197^{\circ}$
17	C_6H_5	$2,4\text{-}Cl_2\text{-}C_6H_3$	$200\text{-}205^{\circ}$
19	$4\text{-}CH_3O\text{-}C_6H_4$	$2,4\text{-}Cl_2\text{-}C_6H_3$	$182\text{-}185^{\circ}$
21	C_6H_5	$2\text{-Cl-}4\text{-}H_5C_2O_2C\text{-}C_6H_3$	$163\text{-}166^{\circ}$

TABLE V (B)

Compound	Mass Spectral Data[a]		IR Frequencies (μ)
	M^+[b,c]	Base Peak	
6	215, 217	215	3.85, 4.28, 5.05, 6.10
7	215, 217	215	3.90, 4.30, 6.15
9	241, 243	240	4.30, 5.08, 6.12, 6.23
10	241, 243	240	4.25, 5.00, 6.15, 6.28
12	260, 262	51	3.88, 5.02, 6.32
15	229, 231	77	3.85, 5.00, 6.32
17	249, 251, 253	161	3.90, 4.30, 6.25
19	279, 281, 283	245	3.90, 6.24
21	287, 289	154	3.88, 5.78, 6.25

TABLE V (B)

a) All mass spectra were observed at 70 ev with a trap current of 100 μA.

b) As is common with hydrochlorides, the highest m/e peak observed involves loss of HCl from the parent molecule.

c) Appropriate Cl isotope patterns were observed in all cases.

d) Melting points of dehydrates.

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13. Takamizawa et al.(ref. 10) have shown that potassium thiocyanate catalyzes the isomerization of alkoxycarbonyl thiocyanates (3) to alkoxycarbonyl isothiocyanates (4).

14. Best results were obtained from a 20' X 3/8" SE column at 350° C.

15. This change in the product ratio is due to the isomerization of the initially produced ethyl thiocyanate to ethyl isothiocyanate. This was verified by exposing ethyl thiocyanate to the experimental conditions.

16. The mechanism of the vapor phase isomerization of alkyl thiocyanate to alkyl isothiocyanates has been investigated by Fava, Macoll and co-workers. Their results indicate a unimolecular, cyclic transition state. However, the substantial amounts of olefin observed in their study contrast so strikingly with our results that it appears their results are not applicable to our system. This should not be surprising, however, since their system was devised to produce *minimum* interactions with the hot surface for convenience in studying the kinetics of the reaction. Our system, on the other hand, was devised for synthetic purposes and allows significantly more interaction with the hot surface. For further details see N. Barrocta, A. Maccoll, M. Cavazza, L. Congru and A. Fava, *J. Chem. Soc.*, *B*, 1264 (1971); *ibid.*, 1267 (1971).

17. For example, see H. Kofod, *Org. Syn.*, *35*, 66 (1955).

18. The facile isomerization of secondary and tertiary alkyl thiocyanates under our experimental conditions appears to be a general phenomenon. Other results of this laboratory using a number of other secondary and tertiary alkoxycarbonyl thiocyanates and isothiocyanates indicate the presence only of N-substituted products.

19. The general method of conversion of a secondary or tertiary alcohol to an amine (the usual precursor to an isothiocyanate) is by means of the Ritter reaction. However, since this process involves a carbonium ion, rearrangement products are often observed. See J.J. Ritter and J. Kalish, *J. Amer. Chem. Soc.*, *70*, 4048 (1948).

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33. (a) D. Liotta, A.D. Baker, F. Weinstein, D. Felsen, R. Engel, and N.L. Goldman, *J. Org. Chem.*, *38*, 3445 (1973); (b) presented in part at the 5th Annual Northeast Regional Meeting, American Chemical Society, Rochester, New York, October 16, 1973, paper number 152.

34. (a) S.R. Sandler and W. Karo, "Organic Functional Group Preparations", Volume 12-III, Academic Press, N.Y., 1972, pp. 301-317; (b) see also refernce 25.

35. Previous work has shown that attempts to prepare nitrones from aldehydes containing an α-hydrogen atom often lead to isoxazolidines effectively through self-condensation of the nitrone: A.D. Baker, J.E. Baldwin, D.P. Kelly, J. DeBernardis, *Chem. Commun.*, 344 (1969).

36. The addition of chlorine to benzylidene aniline was reported in the early literature, but the products were not characterized; see T.C. James and C.W. Rudd, *J. Chem. Soc.*, 105 (1914).

37. Subsequent treatment of the filtrate with hydrogen chlor-

ide caused precipitation of the remainder of imines in solution as their hydrochlorides. These were shown to be, again, an approximately equal mixture of benzylidene aniline hydrochloride and benzylidene *para*-chloroaniline hydrochloride.

38. Whether Intermediate II exists in the form shown or as PhCH(Cl)N(Cl)Ph is irrelevant. The same chlorinated imine hydrochloride should be formed as α-chloroamines readily isomerize to imine hydrochlorides.

39. (a) P. Haberfield and D. Paul, *J. Amer. Chem. Soc.*, *87*, 5502 (1965); (b) *another example is given by* R.S. Neale, R.G. Schepers, and M.R. Walsh, *J. Org. Chem.*, *29*, 3390 (1964).

40. The small amount of *para*- isomer observed in some cases can be accounted for by an S_N2' type process to which Intermediate III might be subject.

41. The reaction procedure was bases on the method described by A.C. Cope and E. Ciganek, *Org. Syn.*, *Coll. Vol. IV*, 339, 612 (1963).

42. J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure". McGraw Hill, N.Y., 1968, p. 431.

43. For comparison purposes, iodobenzene dichloride was prepared by the accepted procedure; H.J. Lucas and E.R. Kennedy, *Org. Syn.*, *Coll. Vol. III*, 482 (1955).

44. O.H. Wheeler and P.H. Gore, *J. Amer. Chem Soc.*, *78*, 3363 (1956).

45. (a) G.E. Utzinger and F.A. Regenass, *Helv. Chim. Acta*, *37*, 1892 (1954); (b) J.H. Bowie, R.G. Cooks, and G.E. Lewis, *Aust. J. Chem.*, *20*, 1601 (1967).

46. B.S. Larsen, B. Soegaard, G. Schroll, S.O. Lawesson, and J.H. Bowie, *Chem Ind. (London)*, 321 (1968); B.S. Larsen, G. Schroll, S.O. Lawesson, J.H. Bowie, and R.G. Cooks, *Tetrahedron*, *24*, 5193 (1968).

47. All elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, New York.

48. The pertinent references for prior preparation of these imines are: (a) V. deGaouck and R.J.W. LeFevre, *J. Chem. Soc.*, 741 (1938); (b) C.F. Winans, *J. Amer. Chem. Soc.*, *61*, 3564 (1939); (c) G. Fench and A. Tommasini, *Atti*

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49. F.C. Schmelkes and M. Rubin, *J. Amer. Chem. Soc.*, *66*, 1632 (1944).

50. I Heilbron, "Dictionary of Organic Compounds", Oxford University Press, New York, 1953, p. 493.

51. *Ibid.*, p.126

52. C. Pouchert, "The Aldrich Library of Infrared Spectra", Aldrich Chemical Co., Inc., Milwaukee, Wis., 1970, p. 545C.