THE PREPARATION AND INVESTIGATION OF SOME HETERO-ATOM ONIUM IONS AND THEIR USE IN ORGANIC SYNTHESIS

by

DAVID C. CHAPMAN, B.Sc.

A Doctoral Thesis submitted in partial fulfillment of the requirements for the award of Doctor of Philosophy of the Loughborough University of Technology

1984

Supervisor: H. Heaney, B.A., Ph.D., D.Sc., F.R.S.C.
Department of Chemistry

To Alison

Summary

A short review of cases where acyl- or alkoxycarbonyl onium salts have been prepared or postulated as intermediates is presented.

The reaction of trialkylamines with chloroformate esters and acyl halides has been re-examined. Chloride ion proved to be too nucleophilic an anion to be able to isolate the salts. The route of decomposition is discussed in detail. The reaction of amines with chloroformates in the presence of antimony pentachloride has been investigated. Chloride ion exchange using triethyloxonium tetrafluoroborate has been achieved in the reaction of phenyl chloroformate with triethylamine, and the ^{13}C nmr spectrum of this salt is discussed in detail.

Several *N*,*N*-dialkylamides and *N*,*N*-dialkylcarbamates have been alkylated using trialkyloxonium tetrafluoroborates. Alkylation on both the carbonyl oxygen and the nitrogen is seen and the ^{13}C nmr spectra of these products are presented.

The reaction of acyl halides with sulphides in the presence of antimony pentachloride has been re-investigated. No acylsulphonium salts have been isolated although evidence for their presence as intermediates is presented. The reactions of acyl halides with sulphides in the presence of silver hexafluoroantimonate or silver tetrafluoroborate are also described. The equivalent reactions using chloroformate esters instead of acyl halides have been investigated. Neither of these routes yields a stable acyl- or alkoxycarbonylsulphonium salt although some decomposition products do indicate that they have been formed at some stage and have been hydrolysed.

Alkylation of several thiocarboxylic acid esters and thiocarbonic acid esters using trialkyloxonium tetrafluoroborates indicates that alkylation occurs predominantly on the sulphur atom. The thiocarboxylic acid esters give the carboxylic acid esters by attack of the ether freed from the alkylating agents. S-Ethyl O-phenyl thiocarbonate yields phenoxycarbonyldiethylsulphonium tetrafluoroborate. The ^{13}C nmr spectrum is presented.

The reaction of acyl halides with ethers in the presence of antimony pentachloride has been re-investigated. The results of F. Klages et al. could not be repeated, i.e. no acyldialkyloxonium salts have been isolated.

The alkylation of several carboxylic acid esters and carbonic acid esters using trialkyloxonium tetrafluoroborates has been examined using ^{13}C nmr techniques. γ-Butyrolactone has been alkylated on the carbonyl oxygen to give a cyclic carbenium ion. The carbonic acid esters appear to undergo no alkylation under similar conditions.

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to my supervisor, Dr. H. Heaney, for his friendly inspiration, guidance and enthusiasm throughout the course of this work.

I would also like to thank Professor P.H. Plesch (University of Keele) for his help and guidance in the design of the vacuum apparatus used in part of this work.

I am indebted to all the staff, both academic and technical, of the Chemistry Dept., but especially to Mike Harrison for running the many ^{13}C nmr spectra reported here.

I would like to thank the Science Research Council for the provision of a maintenance grant.

Thanks also go to my typist for the final preparation of this manuscript.

CONTENTS

CHAPTER 1

INTRODUCTION

1. INTRODUCTION

Hetero-atom onium salts are widely used synthetic tools in organic chemistry. Although there are numerous types of these salts, the three that will be discussed in this work are ammonium salts ($\overset{+}{N}R_4X^-$), sulphonium salts ($\overset{+}{S}R_3X^-$) and oxonium salts ($\overset{+}{O}R_3X^-$).

Ammonium salts have been known since the last century and are often crystalline solids that are stable at room temperature. Tetraalkylammonium salts (1) are easily formed by the Menschutkin

$$R_3N + R'Hal \longrightarrow R_3\overset{\oplus}{N}R' \; Hal^{\ominus}$$

(1)

reaction[1] between tertiary amines and an alkyl halide. Reviews of their reactions can be found in most organic chemistry text-books.

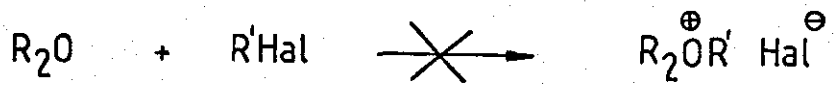
Tertiary sulphonium salts (2) have also been known since the last century[2] and are generally crystalline solids that are stable

$$R_2S + R'I \longrightarrow R_2\overset{\oplus}{S}R' \; I^{\ominus}$$

(2)

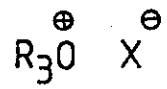
at room temperature. They are prepared by the reaction of alkyl iodides on dialkyl sulphides. The importance of sulphonium salts in synthetic organic chemistry is well-recognised and several recent reviews are available[3,4,5] which cover the many types of sulphonium salts that can be prepared.

Trialkyloxonium salts (3) cannot be prepared by the simple reaction of an alkyl halide with a dialkyl ether. Indeed, for many years it



(3)

was thought that such compounds could not be formed at all. Meerwein[6,7] has reported that such salts (4) are only isolable when relatively non-



(4)

R = alkyl.

X = BF_4, $SbCl_6$.

nucleophilic counter-ions such as BF_4^- and $SbCl_6^-$ are present. These salts give dialkyl ethers and alkyl halides in the presence of halide ions, hence the reason why trialkyloxonium salts cannot be formed by the route shown above, i.e. they act as alkylating agents in the presence of nucleophiles. Reviews on the preparation and use of this type of salt have been presented by Perst[8], Meerwein[9] and Baggett[10].

The stability of trialkyloxonium salts (4) is much lower than that of trialkylsulphonium salts (2). This difference in stability can be explained using R.G. Pearson's theory of hard and soft acids and bases[11], where the "alkyl cation" ("soft" acid) adds more readily to dialkyl sulphides (soft bases) than to dialkyl ethers (hard bases).

The stability of these salts also depends on the counter-ion that is present. Indeed, it has already been mentioned that trialkyloxonium salts can only be isolated when relatively non-nucleophilic anions are used, i.e. those that keep their integrity. The stability of these anions decreases as follows[12]:

$$SbF_6^{\ominus} > PF_6^{\ominus} > SbCl_6^{\ominus} > BF_4^{\ominus} > FeCl_4^{\ominus} > AlCl_4^{\ominus} > SnCl_6^{2\ominus}$$

Acylammonium salts have been isolated with tetrafluoroborate[13] (5) and hexachloroantimonate[14] (6) as the counter-ion.

$$R-\overset{\overset{O}{\|}}{C}-Cl + R'_3N \xrightarrow[2.HF/BF_3]{1.\ -78^{\circ}C} R-\overset{\overset{O}{\|}}{C}-\overset{\oplus}{N}R'_3\ BF_4^{\ominus}$$

R=alkyl.

(5)

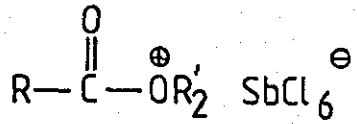
$$R-\overset{\overset{O}{\|}}{C}-Cl + R'_3N \xrightarrow[2.SbCl_5]{1.\ -78^{\circ}C} R-\overset{\overset{O}{\|}}{C}-\overset{\oplus}{N}R'_3\ SbCl_6^{\ominus}$$

R=aryl.
R'=alkyl.

(6)

Such salts have also been prepared by alkylation of N,N-dialkylamides with methyl fluorosulphate followed by rearrangement[15]. These salts are hygroscopic and act as acylating agents with many weak nucleophiles.[13]

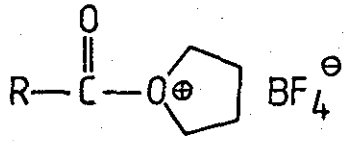
Klages[16] and Meerwein[17] have isolated acyloxonium salts (7) and (8) respectively. These salts are stable only at low temperatures and are susceptible to hydrolysis in the presence of moisture. In the presence of nucleophiles salt (7) acts as an acylating agent. Under



R=Me,Et.

R'=Me,Et.

(7)

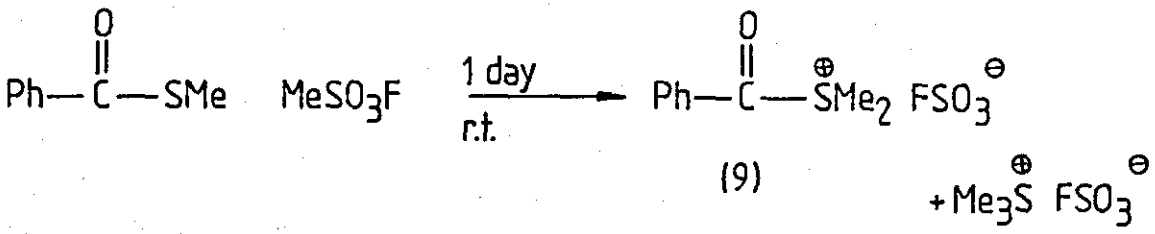


R=Me.

(8)

similar conditions the cyclic salt (8) ring opens, i.e. O-alkyl cleavage takes place.

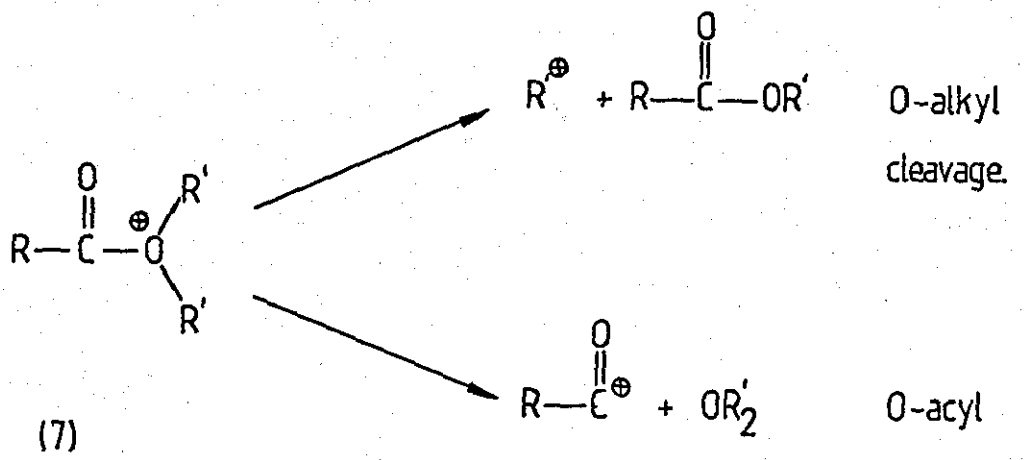
Minato[18] has methylated S-methyl thiobenzoate using methyl fluorosulphate to give benzoyldimethylsulphonium fluorosulphate (9)



(9)

in admixture with trimethylsulphonium fluorosulphate. The salt is stable at room temperature but hydrolyses readily in the presence of moisture. The salt is a powerful acylating agent for various nucleophiles.

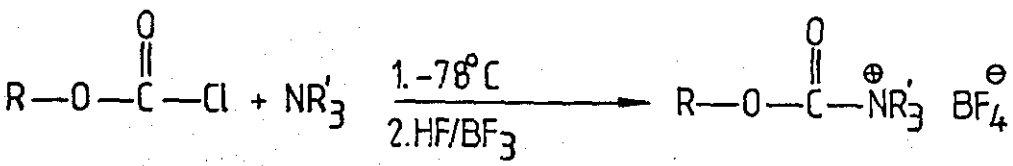
Acylammonium, acylsulphonium and acyloxonium salts can act as either alkyl or acyl donors depending on the reaction conditions, e.g. with (7). The factors affecting this are discussed more fully



(7)

in the following chapters.

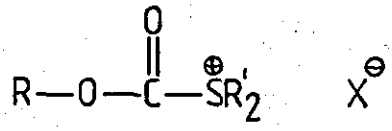
Alkoxycarbonylammonium salts (10) have been prepared by direct



(10) R,R'=alkyl.

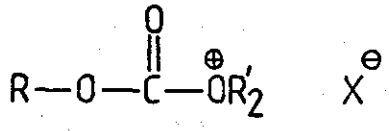
combination of alkyl chloroformates and tertiary amines at low temperatures followed by anion exchange using HF/BF_3[19]. Similar salts have also been prepared in low yield by alkylation of dialkylcarbamates with methyl fluorosulphate[20] followed by rearrangement. Stable salts have been isolated only rarely and are often impure. These salts react with primary and secondary amines to give carbamates in high yields.

There have been no reports of alkoxy/phenoxycarbonylsulphonium salts (11) or alkoxy/phenoxycarbonyloxonium salts (12) in the literature.



(11)

R=alkyl,aryl.
R'=alkyl.
X=BF_4,etc.



(12)

R=alkyl,aryl.
R'=alkyl.
X=BF_4,etc.

In recent years, ^{13}C nmr spectroscopy has been used with considerable success in identifying stable cations in solution. This technique has also enabled the study of the pattern of charge stabilisation in such ions. Nelson[21] has shown that the ^{13}C nmr shifts of phenyl ring carbons in substituted benzenes can be used to monitor changes in charge distribution at those carbons and that the chemical shifts can vary significantly in different solvent systems because of solute-solvent interactions. Olah has done much work on the ^{13}C nmr spectroscopy of stable carbenium ions[22,23,24] and has found the technique invaluable in elucidating structure and charge distribution.

No ^{13}C nmr data has been reported for salts of the type (5) to (12) although data for triacetyloxonium hexafluoroantimonate has been reported by Boekhoff[25].

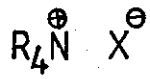
CHAPTER 2

QUATERNARY AMMONIUM SALTS

2.1 Introduction

Quaternary ammonium salts are well-known and well-documented in the literature.

The reaction of alkyl halides with amines readily produces quaternary ammonium salts, although diaryl- and triarylamines are poor nucleophiles. When tertiary amines are used, this reaction is known as the Menschutkin reaction[1]. Alkyl sulphates and sulphonates have also been used in this reaction in place of the halide. Most of these salts (1) are stable at room temperature and can be isolated as



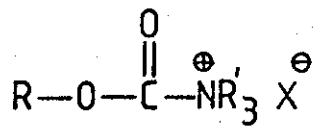
(1)

R=H,alkyl.

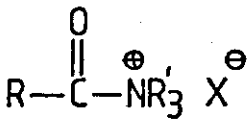
X=Cl,Br,I,etc.

crystalline solids. This contrasts strongly with the equivalent sulphonium and oxonium salts where many may only be isolated when the counter-ion, X^-, is relatively non-nucleophilic, e.g. tetrafluoroborate (BF_4^-), and some are unstable at room temperature.

N-Alkoxycarbonyl- and N-acyl-N,N,N-trialkylammonium salts have been postulated as intermediates in many reactions (see later). Stable salts of the type (10) or (13) have been isolated only rarely and are frequently impure. Paukstelis[13,19] has isolated both types of salt



(10)



(13)

R=alkyl,aryl.

R′=alkyl.

with tetrafluoroborate as the counter-ion. Klages[14] has prepared salts of type (13) with hexachloroantimonate as the counter-ion. Both types of salt have also been prepared by the reaction of methyl

fluorosulphate with either N,N-dialkylcarbamates[20] or N,N-dialkylamides[15] followed by rearrangement, although yields with the latter were generally low at room temperature. These reactions are discussed in more detail in the following sections.

N-Alkoxycarbonyl-N,N,N-trialkylammonium salts (10) have been prepared and studied in connection with the mixed anhydride method of peptide synthesis, where the reaction would be completely free of excess bases (in the formation of the mixed anhydride) that could lead to racemisation[19]. They have also been used successfully for the protection of N-, O- and S-groups.

N-Acyl-N,N,N-trialkylammonium salts (13) have been used as reagents for the preparation of protecting groups[13]. The size of the tertiary amine used in the preparation of the salt can be varied which allows the possibility of stereo-selective acylating agents, especially in reactions with alcohols. Paukstelis' paper[13] describes their reaction with a selection of amines, amides, thiophenols and alcohols.

There appears to be no published work on the ^{13}C nmr spectra of salts of type (10) and (13). Using ^{13}C nmr techniques it is possible to study the effect the positive charge has on the molecule and to ascertain how this change is stabilised.

The sections that follow describe in detail the work carried out by the author in order to characterise the salts (10) and (13). Several methods of preparation were investigated which are described in section 2.2.

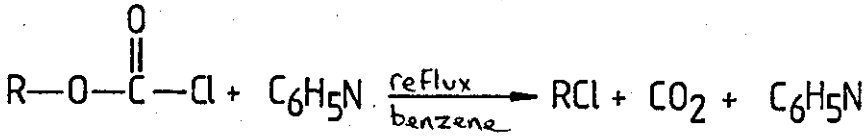
These salts are all hygroscopic, readily decomposing on contact with moisture. Much of the early work carried out was hindered considerably by this problem. Considerable time was spent developing techniques and apparatus which ensured anhydrous conditions (see experimental). Many of the reactions between chloroformate esters and amines were conducted on a vacuum-line as these compounds were extremely susceptible to hydrolysis. Full experimental details are given in Section 2.3.

2.2 Preparation and Reactions of α-Carbonyl Ammonium Salts

2.2.1 Reaction of chloroformates with amines

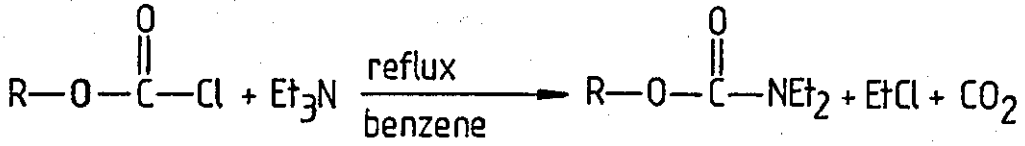
The reactions of chloroformates with amines are well-known[26,27,28] and have been used in many synthetic routes. These are many and varied as can be seen by the following examples.

Ethyl chloroformate reacts with quinoline and pyridine in ether to give a yellow compound and a red compound respectively[29]. Decomposition in water gives ethyl chloride, ethanol, carbon dioxide, the free base, and the hydrochloride of the base. Reflux of pyridine with ethyl chloroformate in benzene gives the alkyl chloride, carbon dioxide and the free base[30], (equation 1).



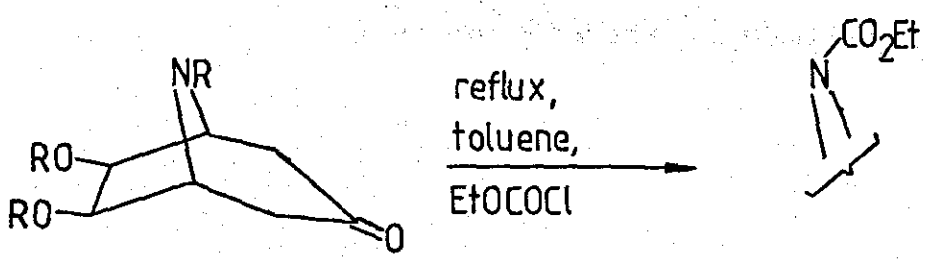
(equation 1)

With trialkylamines such as triethylamine , ethyl chloride, carbon dioxide and N,N-diethylethyl carbamate are formed on reflux in benzene[27] (equation 2):



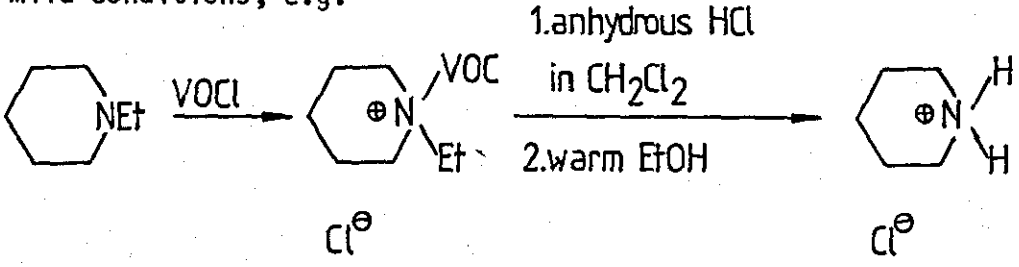
(equation 2)

This latter reaction is often utilised in the dealkylation of tertiary amines and has been found superior to the von Braun cyanogen bromide reaction in many cases because of increased selectivity which produces cleaner reactions[31,32,33].



Ref: 31.

However, the carbamate product is not easily hydrolysed and can require prolonged reaction times in the presence of strong acids or bases. The use of phenyl chloroformate can partially overcome this problem, but the use of 2,2,2-trichloroethyl chloroformate[34] or vinyl chloroformate [35,36] gives a selective dealkylation under mild conditions, e.g.



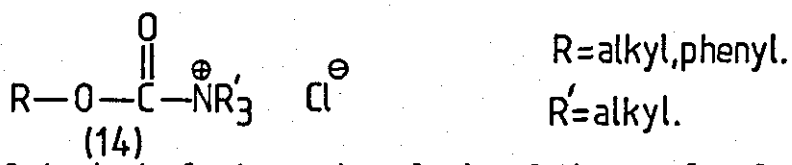
Ref: 36.

Phenyl chloroformate in the presence of a mild base[36] has been used for N-demethylation of 6,7-benzomorphans[37], codeine[37] and morphine[38]. N-Dealkylation of cyclic systems has been achieved in many other molecules whilst retaining the cyclic structure[26,29,40,41,42], although ring cleavage has also been seen in some instances[43].

Hobson[26] reported that phenyl chloroformate reacts on reflux in dichloromethane with tertiary amines such as tri-n-butylamine and N-methylpiperidine to give the corresponding carbamate in high yield. In the latter example the piperidine ring is not cleaved which contrasts with the von Braun cyanogen bromide cleavage reaction[44].

Benzyl chloroformate is well-known for its usefulness as a protecting group in peptide chemistry[45], and need not be discussed further here.

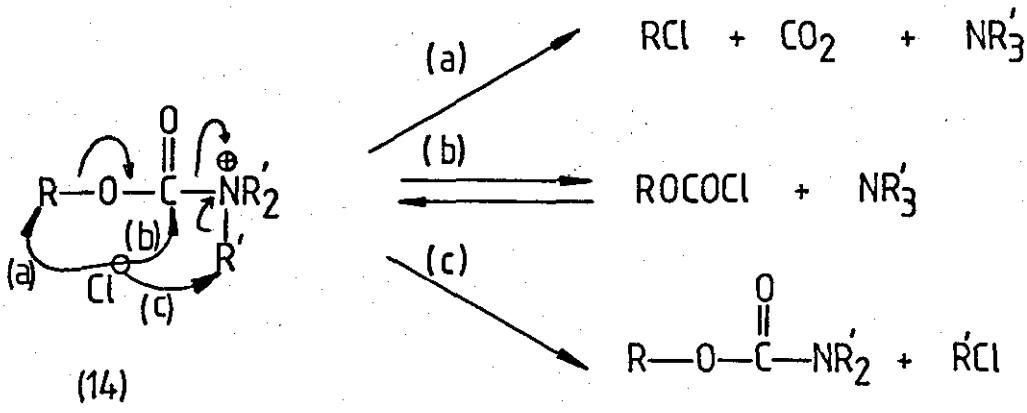
All these reactions of chloroformates with trialkylamines involve a N-alkoxycarbonyl-N,N,N-trialkylammonium salt intermediate , although the salts were not isolated as such in most cases.



(14)

Indeed, isolation and analysis of these salts frequently showed that the substances were mixtures[19]. Also the chloride ion is a strong enough nucleophile to make the reaction reversible to a small extent.

The salts (14) are known to decompose by three routes:[26,27]



(14)

Route (a) is suppressed by using phenyl chloroformate rather than an alkyl chloroformate. We have already mentioned that the reaction is somewhat reversible, route (b). Route (c) is the preferred route when R = phenyl and is the major route in the reactions mentioned above.

Although the chloride ion appears to be a strong nucleophile it was decided to investigate some of these "crude" salt-mixtures. Reaction of phenyl chloroformate with a trialkylamine is known to give an isolable solid in solvents such as benzene or toluene[26], and was thus chosen as the most suitable chloroformate ester.

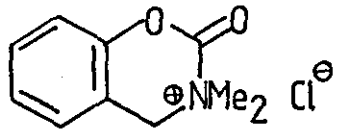
The reactions of phenyl chloroformate with trimethylamine and triethylamine are discussed at length in sections 2.2.1.1 and 2.2.1.2 respectively. The reaction of N-phenoxycarboxy-N,N,N-triethyl ammonium chloride with various nucleophiles was investigated.

These early results showed that the salts formed were extremely susceptible to hydrolysis. An experimental procedure using a vacuum system was developed which eliminated many of these problems.

Reaction of phenyl chloroformate with N,N-dimethylbenzylamine and N-methylpiperidine (sections 2.2.1.3 and 2.2.1.4) gave salts that could not be isolated other than in ether or toluene. Preparation in dichloromethane followed by decomposition in situ resulted in the expected products, i.e. carbamates.

Section 2.2.1.5 describes the reaction of N-methyltetrahydroisoquinoline with phenyl chloroformate in dichloromethane. This shows an unusual decomposition pattern in that the expected ring cleavage at the benzylic position does not occur, and the amine is demethylated.

The reaction of phosgene with 2-(dimethylaminomethyl)phenol is described in section 2.2.1.6. The salt (15) is postulated as an intermediate but was not isolated.



(15)

These reactions are discussed fully in the sections that follow.

2.2.1.1 Reaction of phenyl chloroformate with trimethylamine

Reaction in dry benzene gave a hydroscopic colourless solid in almost quantitative yield. Attempts to obtain spectra resulted in rapid decomposition/hydrolysis, presumably by trace amounts of water, to give the expected products, i.e. diphenyl carbonate and trimethylamine hydrochloride.

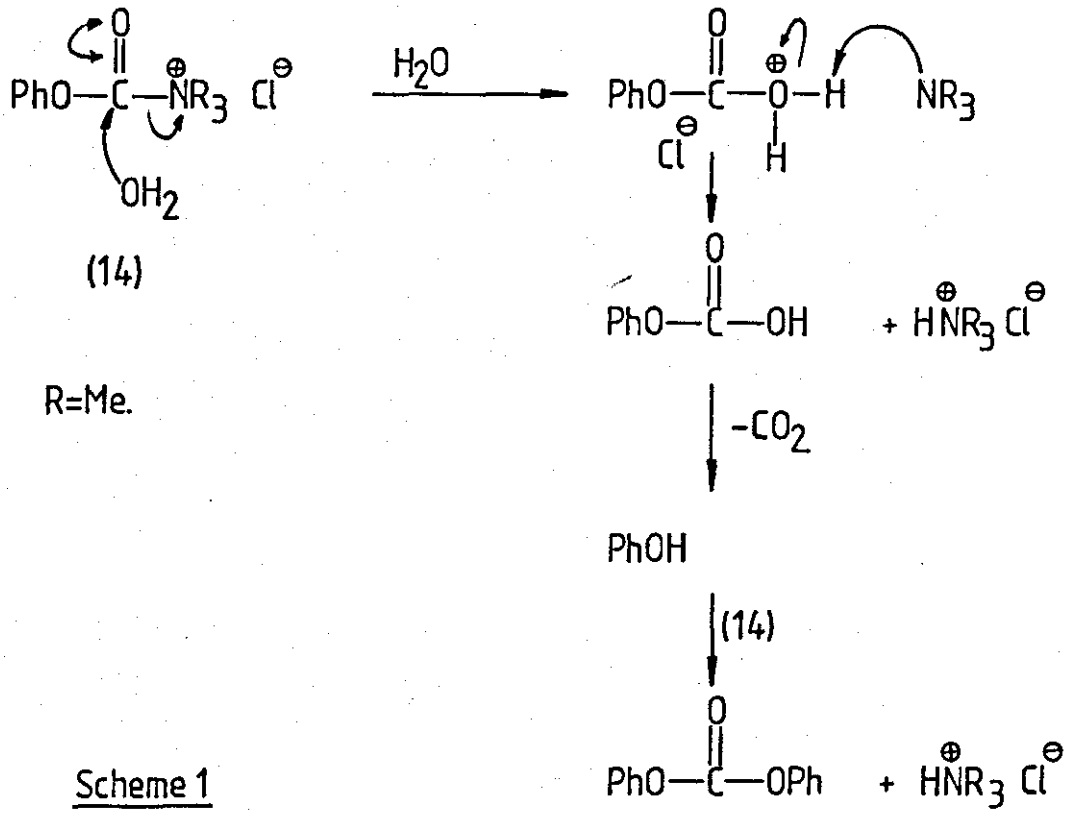
A similar result was achieved when the solid was refluxed in benzene for 24 hours without protection from atmospheric moisture. A quantitative yield of the amine hydrochloride was formed together with diphenyl carbonate in approximately 50% yield.

Decomposition of the solid in dichloromethane at room temperature over 12 hours gave similar results.

Phenyl chloroformate itself is not susceptible to hydrolysis under these mild conditions.

No products connected with the nucleophilic attack of the chloride ion on the salt were isolated in these reactions.

The following mechanism for hydrolysis of the salt is proposed (scheme 1):



Scheme 1

It was not possible to characterise salt (14) under these conditions.

2.2.1.2 Reaction of phenyl chloroformate with triethylamine

Reaction of phenyl chloroformate and triethylamine in dry benzene gave a colourless solid in 66% yield. Attempts to obtain spectra of the solid were unsuccessful due to rapid hydrolysis to give diphenyl carbonate and triethylamine hydrochloride.

Preparation in dry benzene followed by decomposition in situ at reflux temperature gave phenyl N,N-diethylcarbamate in 97% yield, together with a small amount of diphenyl carbonate formed by hydrolysis of the salt.

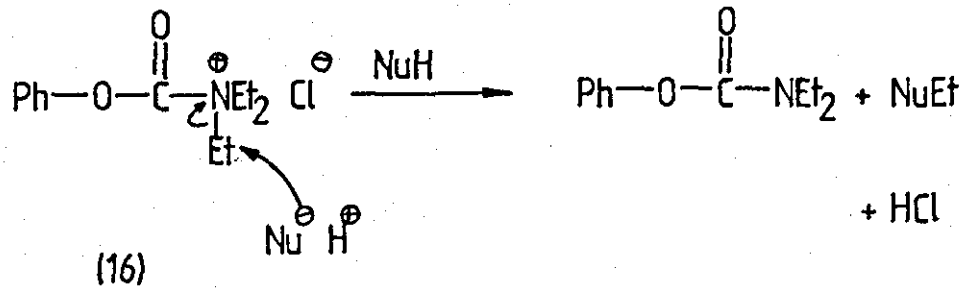
When dichloromethane was used as the solvent decomposition was achieved at room temperature to give the carbamate in 94% yield, with a small amount of diphenyl carbonate.

In order to exclude as much moisture as possible a vacuum-line was used in several experiments. The preparation was carried out in ether, and the product was then decomposed in dry methylene chloride. This gave a 90% yield of the expected carbamate and also a small amount of diphenyl carbonate. The low yield was due to loss of the product by evaporation during the removal of solvent at the work-up stage.

These results indicate that the salt is extremely susceptible to hydrolysis by nucleophilic attack by water at the carbonyl group. The mechanism for this hydrolysis is as shown in Scheme 1 above (section 2.2.1.1), where R = Et.

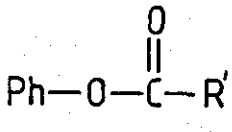
In order to further investigate this reaction with nucleophiles, the salt was reacted with a series of nucleophiles using identical reaction conditions. The results are tabulated in Table 1.

However, it is evident from the reaction with thiophenol that an alternative attack is also occurring:



(16)

Table 1

Nucleophile	Products		
			$HNEt_3\,Cl$
Ethanol	R' = OEt	90%	84%
	R' = NEt_2	5%	
Phenol	R' = OPh	90%	approx. quantitative
	R' = NEt_2	5%	
t-Butyl alcohol	R' = NEt_2	> 90%	-
	R' = OPh	< 5%	
Ethanethiol	R' = SEt	85%	86%
	R' = NEt_2	< 5%	
	R' = OPh	< 5%	
Thiophenol	R' = SPh	approx 80%	86%
	R' = NEt_2	< 5%	
	R' = OPh	< 5%	
	+ Ph – S – Et		

Indeed, with each of these reactions the carbamate was isolated in low yield which suggests that this is a competing reaction to the main one. The alkylated nucleophiles in the other reactions were not isolated presumably because they were too volatile and were evaporated off with the solvent at the work-up stage.

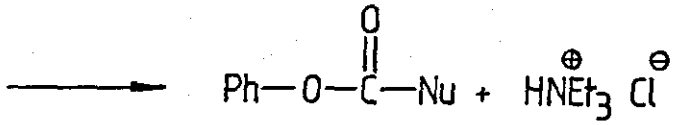
With t-butyl alcohol the major product was the carbamate. There are two possible explanations. The first explanation is that as t-butyl alcohol is a very weak nucleophile, it can only dealkylate the salt by the route outlined above (no tests for the presence of t-butyl ethyl ether were carried out). The alternative explanation is that

the salt partially dissolved in the t-butyl alcohol/ether solution making decomposition by attack of chloride ion the predominant reaction. This latter explanation is the most likely as with the former reaction we would still expect to see some t-butyl phenyl carbonate isolated - this was not observed.

Small amounts of diphenyl carbonate were formed in these reactions, presumably by hydrolysis, even though they were carried out using a vacuum-line.

The reaction of phenyl chloroformate with each of these nucleophiles was checked using identical reaction conditions. Only with phenol, ethanol and ethanethiol was there any noticeable reaction. Phenyl chloroformate was recovered in almost quantitative yield with the other nucleophiles. Where reaction had taken place it was estimated that in no case was the reaction more than 50% complete, ethanol being the most nucleophilic of the group.

These results show that the salt is attacked at the carbonyl group by most nucleophiles to give the expected product and triethylamine hydrochloride, i.e.

(16) 

2.2.1.3 Reaction of phenyl chloroformate with N,N-dimethylbenzylamine

Reaction in dry ether yielded a colourless, sticky solid which readily decomposed on isolation and exposure to the atmosphere. No spectra were recorded. This solid seemed to be partially soluble in ether at room temperature, and evaporation of the ether gave an 83% yield of phenyl N,N-dimethylcarbamate and benzyl chloride. Indeed, when the reaction was repeated using the vacuum-line an almost quantitative yield of these products was isolated.

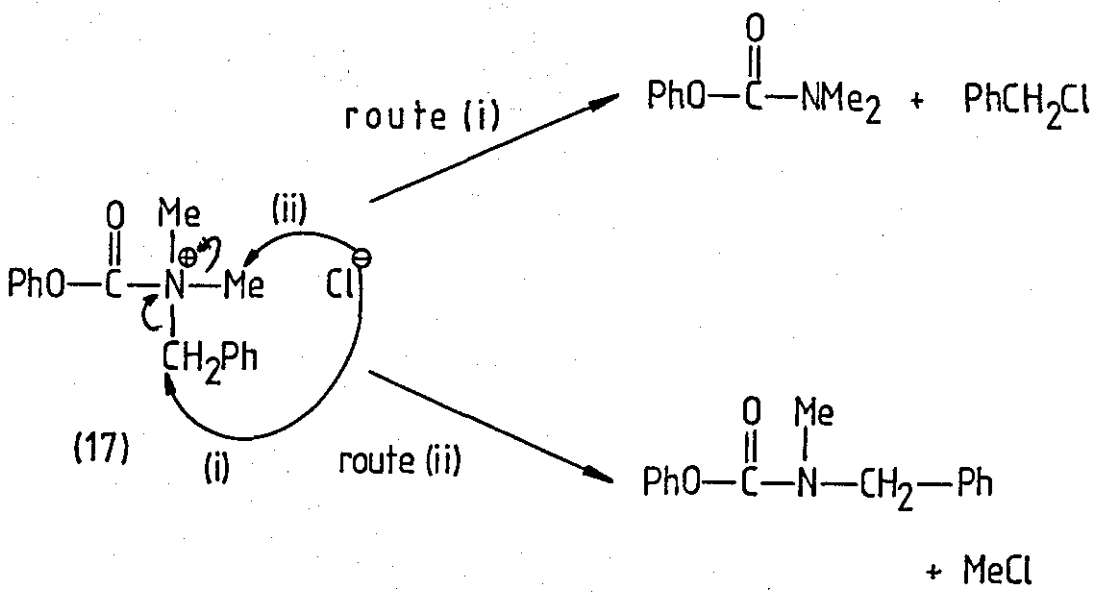
When dichloromethane was used as the solvent the same decomposition products were formed but the reaction did not go to completion as phenyl chloroformate could be identified in the product mixture.

Reaction of neat phenyl chloroformate with neat N,N-dimethylbenzylamine gave a quantitative yield of benzyl chloride and phenyl N,N-dimethylcarbamate after only five minutes.

Preparation in dry toluene gave similar results to those achieved in ether with an overall yield of 82% (by weight). When the salt was prepared in toluene and decomposed in situ at reflux, the same major products were formed as well as phenol and N,N-dimethylbenzylamine hydrochloride in very low yield.

Preparation in ether followed by the addition of water gave benzyl chloride and phenyl N,N-dimethylcarbamate in 85% yield. This unexpected result is explained later.

Thus it can be seen from these results that cleavage of the benzyl group by the chloride ion (route (i)) is preferred to the cleavage of the methyl group (route (ii)).

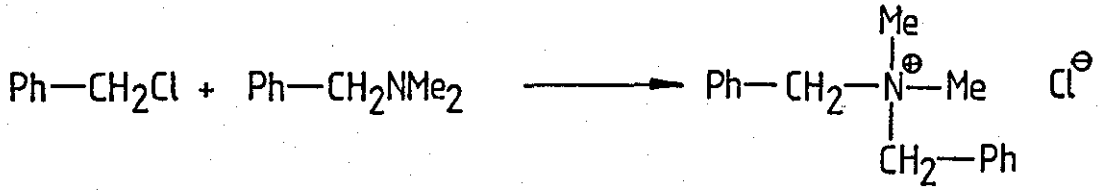


This is certainly due to the inherent stability of the benzyl cation compared to that of the methyl cation. A similar benzyl cleavage has been reported by Douglas[46] in synthesis of heterocyclic compounds using cyclopropionyl chloride in refluxing toluene, and by Ziegler[42,47].

There seem to be no literature examples of cleavage by route (ii). The author has identified two such reactions and these are described in sections 2.2.1.5 and 2.2.1.6.

It is possible that the slight solubility of the salt (17) in ether enabled decomposition to take place as soon as it was formed, and isolation of salt (17) proved to be impossible. Indeed, evaporation of the ether caused the salt to become soluble in the products already formed, thus enabling complete decomposition to take place - the solid salt was never isolated as such.

The salt was readily soluble in dry dichloromethane. This facilitated decomposition by route (i) above, even though at room temperature the reaction did not go to completion as some phenyl chloroformate was isolated. This is possibly due to the benzyl chloride formed in the decomposition reaction reacting with some unchanged N,N-dimethylbenzylamine to give a quaternary salt (18) - this was not verified as any quaternary salts formed were not isolated during the work-up.



(18)

The results using toluene as solvent again show that decomposition by route (i) is preferred. However, on refluxing in toluene two minor products were isolated, i.e. N,N-dimethylbenzylamine hydrochloride and phenol. These were formed by hydrolysis of the salt by minute amounts of moisture in the reaction vessel.

This result seems to conflict with the result achieved when a large amount of water was added to a toluene suspension of the salt. This yielded the carbamate and benzyl chloride in approximately 85% yield, rather than the expected hydrolysis products of phenol and the amine hydrochloride. This can be explained by assuming that the dealkylation reaction by chloride ion is much faster than the hydrolysis reaction. Also, as the salt (17) is very soluble in the excess water present, it readily decomposes by route (i) to give the products described above.

2.2.1.4 Reaction of phenyl chloroformate with N-methylpiperidine

This reaction was carried out in ether. A solid was initially formed, but this decomposed rapidly to many unidentifiable products when attempts were made to isolate it.

However, when the salt was prepared and decomposed in situ in dry dichloromethane at room temperature, phenyl piperidinylcarbamate was isolated in 81% yield.

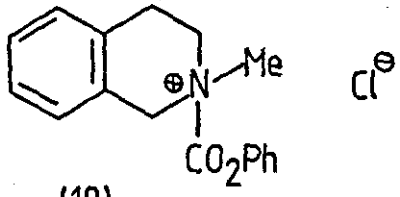
This latter result matches that reported by Hobson[26], decomposition occurring by nucleophilic attack of the chloride ion on the methyl group yielding the carbamate and methyl chloride. No evidence for the opening of the piperidine ring was observed.

Campbell[27] has also found that the reaction of stigmasteryl chloroformate with N-ethyl and N-methyl piperidine gave stigmasteryl N-piperidinylformate, with no evidence of ring opening.

This is in direct contrast with the Hoffman and von Braun reactions where the piperidine ring is opened in amine cleavage.

2.2.1.5 Reaction of phenyl chloroformate with N-methyltetrahydroisoquinoline

No attempt was made to isolate salt (19).



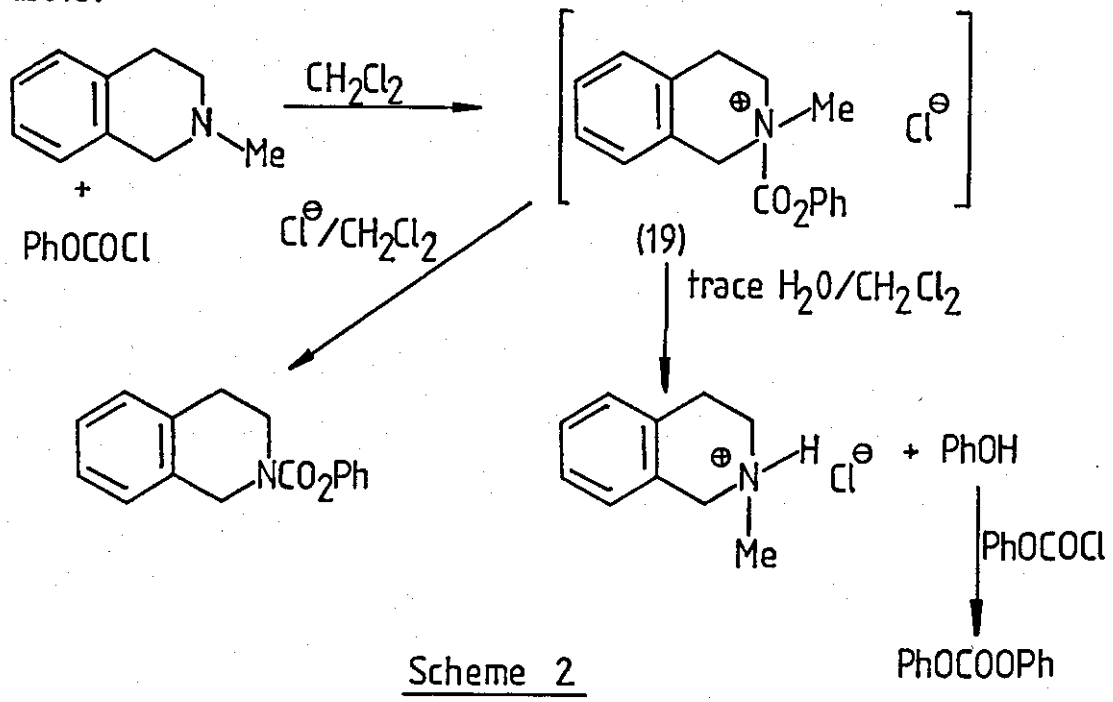
(19)

When the salt was formed and decomposed in situ in dichloromethane at room temperature the major product was N-(phenoxycarbonyl)tetrahydroisoquinoline (59% yield), together with diphenyl carbonate (yield not determined). The work-up procedure did not allow identification of any water-soluble products.

The reaction was repeated using identical conditions and the crude

reaction mixture was analysed after the solvent had been evaporated but before washing with any aqueous solutions. This showed that not only were the products above formed, but also the hydrochloride of the amine was present together with unreacted phenyl chloroformate. The initially expected phenoxycarbonylammonium salt was not present.

It can be deduced from these results that the nucleophilic chloride ion is attacking the methyl group rather than the normally preferred benzylic group. This is in direct contrast to the result with phenyl-chloroformate and N,N-dimethylbenzylamine described in section 2.2.1.3 above.



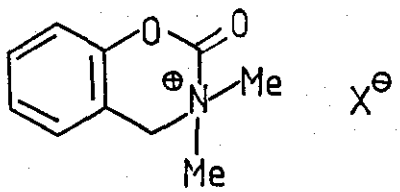
Scheme 2

This is possibly explained by considering steric effects as attack by chloride ion at the benzylic position would appear to be severely hindered. Further evidence for this view is presented in section 2.2. 1.6 below, where ring cleavage at a benzylic position was seen to occur as well as attack at a methyl position. In this connection it was decided to investigate the reaction of phenyl chloroformate with N-methyl-tetrahydroquinoline. However, due to experimental difficulties this work was not completed.

The hydrolysis products from salt (19) were formed by the route shown in Scheme 2. No phenol was noticed in the products but this was because it readily reacts with excess phenyl chloroformate to give diphenyl carbonate.

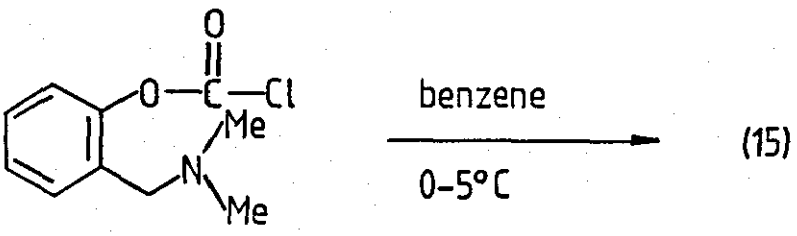
2.2.1.6 Reaction of phosgene with 2-(dimethylaminomethyl)phenol

This reaction was carried out in an attempt to isolate the cyclic phenoxycarbonylammonium salt (15) shown below.



(15)

It was hoped that phosgene would react with the phenol to give the chloroformate ester which could be isolated and then reacted with silver hexafluoroantimonate[48] to give the salt (15) where $X^- = SbF_6^-$ This salt should be more stable than the salt with $X^- = Cl^-$. Initial isolation of the products of this reaction showed that the chloroformate (20) was present (IR C = O (stretch) 1787 cm^{-1}), but this quickly decomposed to give the products shown below. This presumably occurred by intramolecular reaction of (20) to give (15) ($X^- = Cl^-$), which then decomposed by nucleophilic attack of chloride ion to give the two major products.

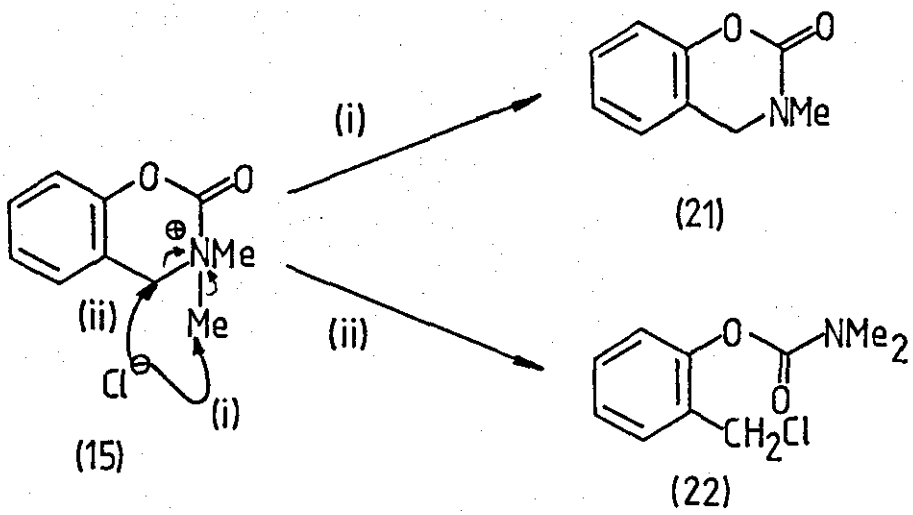


(20)

It was not possible to isolate (15) ($X = Cl^-$). The two major products in this reaction were identified as 3-methyl-2-oxo-dihydro-1,3-benzoxazine (21), and N,N-dimethyl-2-(chloromethyl)phenylcarbamate (22)

by nmr and IR techniques.

These two products can only have been derived from the decomposition of salt (15) by the routes shown below:



These reaction products are somewhat surprising considering the results described in sections 2.2.1.3 and 2.2.1.5 of this chapter.

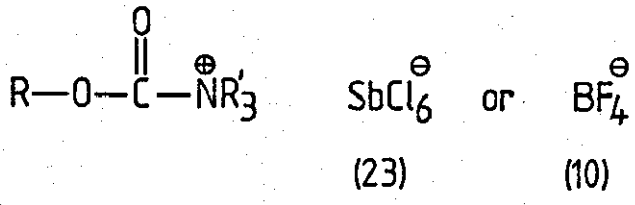
It would be expected that decomposition would proceed only by route (ii) i.e. benzylic cleavage. However, cleavage by route (i) was also observed to give (21).

We have seen that in the reaction between phenyl chloroformate and N-methyltetrahydroisoquinoline nucleophilic attack at the benzylic position did not take place presumably because of severe steric hinderance (section 2.2.1.5). In salt (15) this hinderance is not so severe and nucleophilic attack at the benzylic position does indeed take place. Unfortunately we have no data on the relative ratios of these products, although nmr data suggests that attack is predominantly at the methyl position. This is because attack by chloride ion is still hindered to some extent by the aromatic ring system and the bulky groups attached to the positively charged nitrogen atom.

2.2.2 Reaction of chloroformates with amines in the presence of a Lewis acid

Although the reaction of a chloroformate with a trialkylamine generally produces an N-alkoxycarbonyl-N,N,N-trialkylammonium salt as an

intermediate, the chloride ion is a good nucleophile and can attack the salt to give several products. To eliminate this problem a relatively non-nucleophilic anion is needed, such as hexachloroantimonate ($SbCl_6^-$) (23) or tetrafluoroborate (BF_4^-) (10).

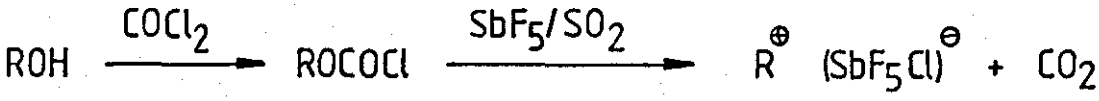


(23) (10)

It has been reported that the chloride ion in N-alkoxycarbonyl-ammonium chlorides can be exchanged for the tetrafluoroborate ion by reaction of the salt with a 1:1 mixture of HF/BF_3 in ether at -78°C[19]. Most of these salts give sharp melting points but vary greatly in their stability.

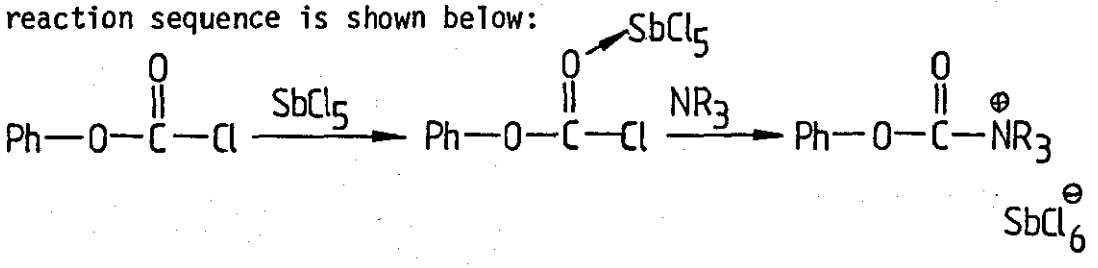
The reaction of acyl chlorides with amines in the presence of antimony pentachloride has been reported to give N-acyl-N,N,N-tri-alkylammonium hexachloroantimonates in high yield[14]. No such reactions involving chloroformates have been reported.

It is known, however, that antimony pentachloride reacts with ethyl chloroformate in ethylene chloride to give ethyl chloride and carbon dioxide[45]. Only traces of hydrogen chloride, which would have accompanied ethylene formation, were observed. Chloroformates have been found to be useful intermediates for generating carbenium ions from primary and secondary alcohols in antimony pentafluoride/sulphur dioxide solution[49].



Alkyl and aryl chloroformates give complexes with antimony pentafluoride in sulphur dioxide or sulphuryl chloride fluoride[49]. The complexes of alkyl chloroformates lose carbon dioxide to give the corresponding alkyl fluoroantimonates. Analysis of these reactions using ^{13}C nmr and ^{1}H nmr techniques failed to identify the alkoxycarbonyl cation as a long-lived species. An aromatic carboxylium ion would not be expected to eject carbon dioxide to give a high energy aryl cation, and can indeed be used as an electrophile in a Friedel-Crafts acylation.

Because of these reactions phenyl chloroformate was selected as the most suitable chloroformate for our needs, i.e. it would not decarboxylate on reaction with antimony pentachloride. The general reaction sequence is shown below:



(24)

Salts of type (24) would be expected to be extremely hygroscopic. Reactions were carried out in a one-piece, custom-built apparatus that enabled the reaction and the isolation of the solid to take place at low temperature under a dry nitrogen atmosphere (see experimental section).

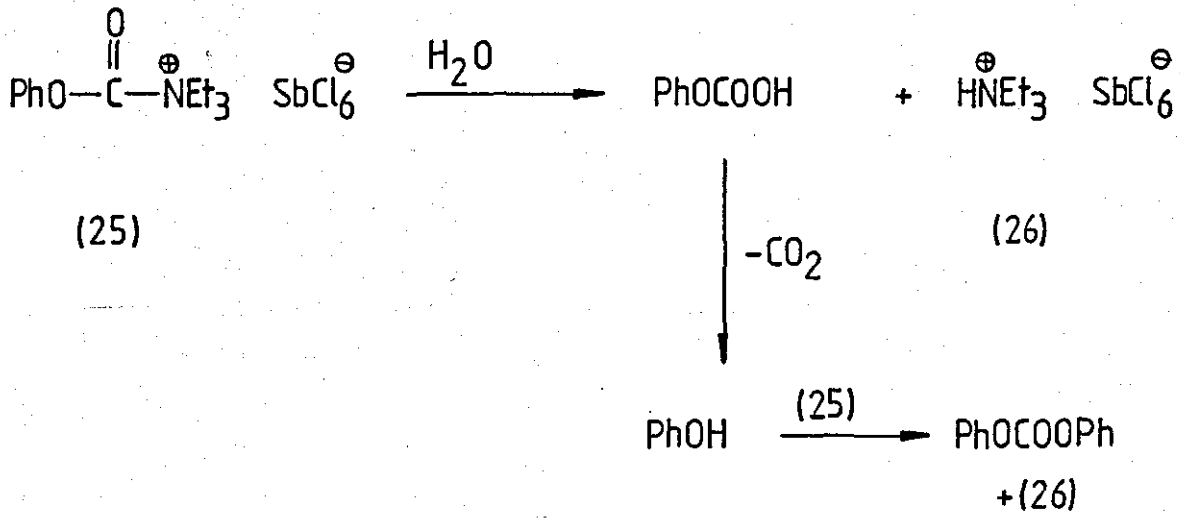
Our results are discussed below.

2.2.2.1 Reaction of Phenyl chloroformate with triethylamine in the presence of antimony pentachloride

Reaction according to the method given in section 2.3.2.1 gave a pale brown solid. This was identified as triethylammonium hexachloroantimonate (29% yield) by comparison with authentic spectra[50]. There was no evidence for the presence of the expected salt (25).

Even though great care was taken to exclude moisture from the reaction, hydrolysis appears to have taken place.

It is postulated that the salt (25) was formed in this reaction and was hydrolysed during the work-up procedure, as shown below.



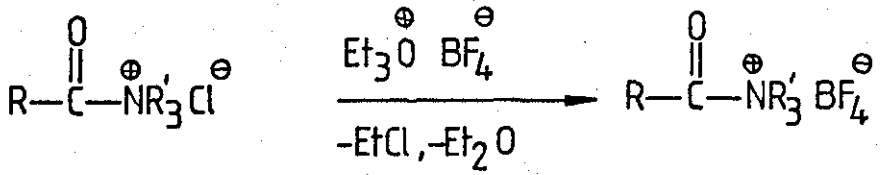
No tests were carried out to verify the presence of phenol or diphenyl carbonate in the filtrates.

Further evidence to back up these findings is presented in section 2.2.1.

2.2.3 Reaction of chloroformates with amines in the presence of triethyloxonium tetrafluoroborate

The reaction of chloroformate esters with amines has already been discussed in detail in section 2.2.1.

Paukstelis[13] has isolated N-acyl-N,N,N-trialkylammonium tetrafluoroborates by reacting an acyl chloride with a trialkylamine at low temperature to give the chloride salt, which was then reacted with triethyloxonium tetrafluoroborate in order to exchange the anion:



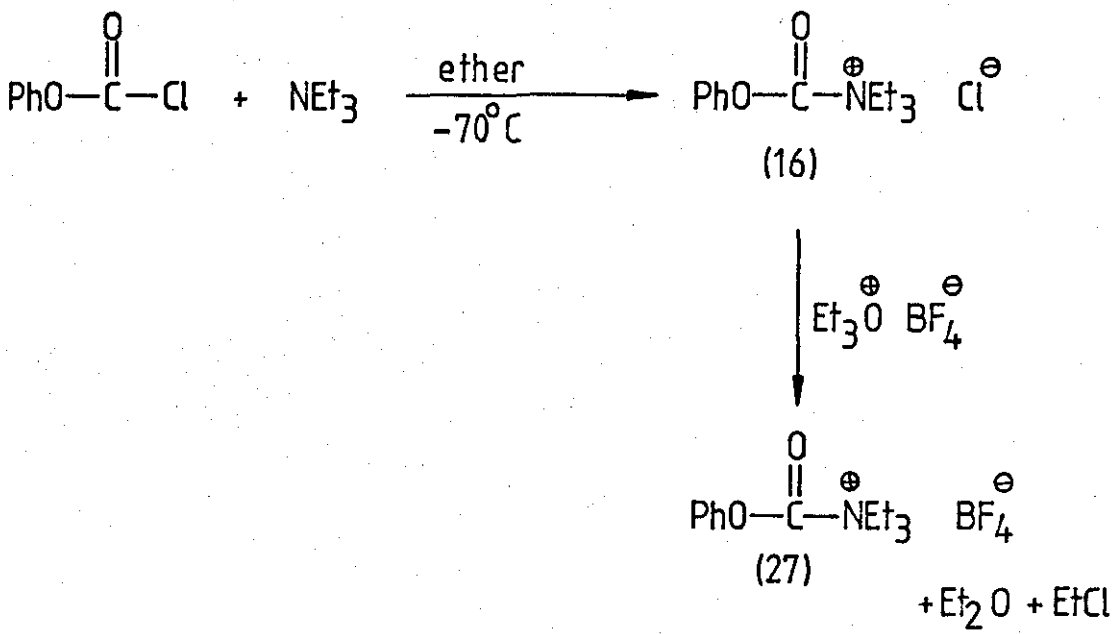
It was decided that this procedure should also work for the N-alkoxy type salts.

No reactions of this type have been reported before.

Our work is described in more detail below.

2.2.3.1 Reaction of phenylchloroformate with triethylamine in the presence of triethyloxonium tetrafluoroborate

Phenyl chloroformate and triethylamine were mixed at -70°C in ether to give the salt (16). This was then treated with triethyloxonium tetrafluoroborate using the method of Paukstelis[13] in order to exchange the chloride ion for the less nucleophilic tetrafluoroborate

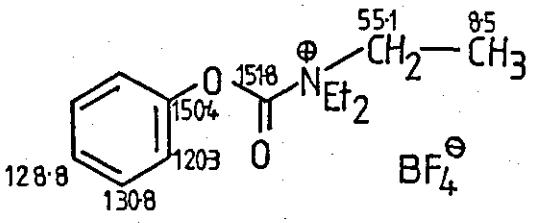


ion. The solid was isolated in 35% yield, and was found to be a mixture of (27) and a triethylammonium salt, probably the tetrafluoroborate. This was formed by hydrolysis of (27). Nucleophilic attack by the chloride ion in (16) was slowed down by keeping the temperature low, and by using ether as the solvent so that (16) precipitated out of solution.

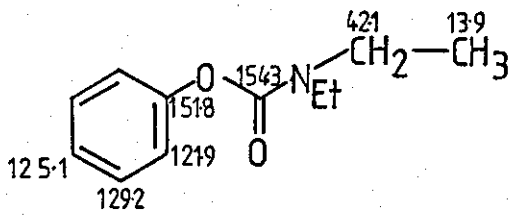
Infrared spectroscopy showed (27) to have a carbonyl stretching frequency of 1822 cm^{-1}. This is in close agreement with values given by Paukstelis[19] for N-alkoxycarbonyl-N,N,N-trialkylammonium tetrafluoroborates. Phenyl chloroformate absorbs at 1787 cm^{-1}. Thus it can be seen that this is increased by 35 cm^{-1} in salt (27). This is also a considerable increase in frequency when compared with phenyl

N,N-diethylcarbamate which has a carbonyl stretching frequency of 1720 cm^{-1}.

The effect of the positive charge on the nitrogen atom was investigated further using ^{13}C and ^{1}H nmr techniques.



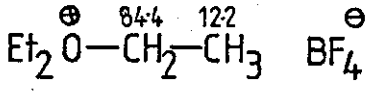
(27)

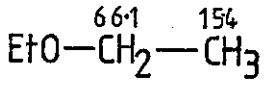


(28)

Comparing (27) with (28) we can detect several important differences.

The methylene carbon in (28) has moved to considerably lower field in (27), whereas the methyl carbon has moved slightly in the opposite direction, i.e. to higher field. A similar effect is obtained when comparing triethyloxonium salts with diethyl ether (see below):





Also it can be seen that although the carbonyl group in (27) is next to the positively charged nitrogen, its chemical shift has not changed significantly. This is explained by the fact that the positive charge cannot be stabilised by the phenoxycarbonyl group as effectively as it can by the alkyl groups present. This argument is strengthened by the fact that there is also little change in the chemical shifts of the aromatic carbons, which would be expected if the positive charge was being partially stabilised by the aromatic ring system.

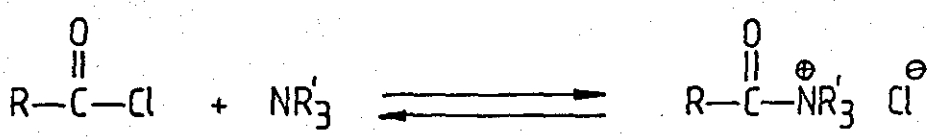
The chemical shifts of the methyl and methylene groups in (27) should also be compared with those in tetraethylammonium salts. In

tetraethylammonium bromide[51] these shifts are 7.4 and 51.9 ppm respectively. This supports the argument above as here the positive charge is stabilised over four alkyl groups rather than three, and thus the effect on the chemical shift of the methylene group is not so pronounced.

Analysis of the proton nmr spectrum verified the above findings. There was little change in the shift for the aromatic protons. The effect of the positively charged nitrogen was noticeable in the shifts of the methylene protons and methyl protons. The methylene protons were seen at δ 3.82 in (27) compared with δ 3.38 in the carbamate, a downfield shift of δ 0.44. The methyl protons were at δ 1.40 in (27) compared with δ 1.21 in the carbamate, a shift of δ 0.19.

2.2.4 Reaction of acyl chlorides with amines

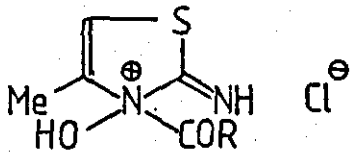
The reaction of an acyl chloride with an amine has been known to produce a stable N-acyl-N,N,N-trialkylammonium salt (13) under certain conditions.



(13)

Preparation in an inert solvent such as ether or benzene at temperatures below 0°C often gives the salt (13) as a white, crystalline material that is easily decomposed by moisture. Such salts have been isolated on many occasions. Examples include: reaction between furoyl chloride and pyridine[52], benzoyl chloride and triethylamine[53], acetyl chloride and pyridine[53], and acetyl chloride and β-picoline[54]. However, on mixing benzoyl chloride with trimethylamine in ether at 0°C no reaction is seen[55].

Stable salts (29) have been isolated in high yield and in a pure state from the reaction of 2-amino-4-methylthiazole-3-oxide with various acyl chlorides[56,57]. The salts have been fully characterised



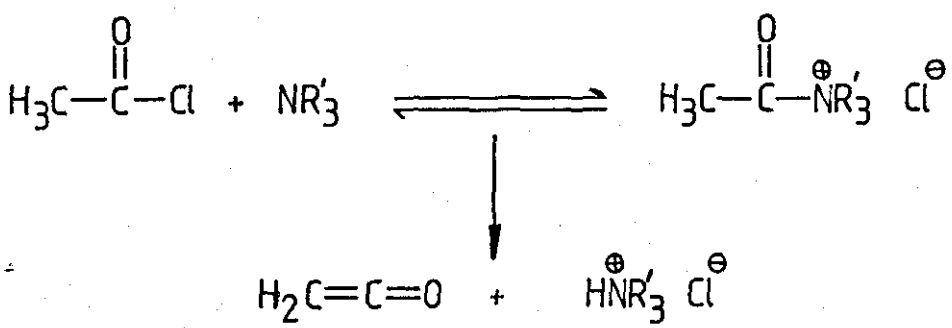
(29)

R=Me,Et,Pr,Ph,Ph—CH_2,

using 'H nmr and IR techniques. The carbonyl stretching frequency varied between 1778 cm^{-1} and 1815 cm^{-1} which is in good agreement with those reported for N-acyl-N,N,N-trialkylammonium salts by Paukstelis[13].

This type of salt has been assumed to be an intermediate in many reactions often followed by nucleophilic attack of the chloride ion to give an amide by dealkylation[46,58,59]. The reaction of acyl chlorides with pyridine in the presence of hydrogen peroxide has been used for the preparation of peroxycarboxylic acids[60].

The salts (13) are highly reactive and are often impure which has made detailed examination of their structures and properties very difficult[61]. It is assumed that the major cause of instability is the nucleophilic chloride ion. This means that the reaction shown below is reversible, enabling dehydrohalogenation by the tertiary amine where an α-hydrogen atom is eliminated from the acyl group, for example:



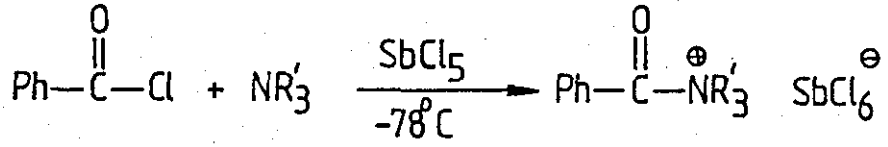
This reaction is known to take place when acetyl chloride is mixed with triethylamine in an inert solvent at room temperature, giving ketene and triethylammonium chloride[62]. Indeed, these hydrohalide impurities are readily seen in the IR spectra of these products as they exhibit a strong absorption in the region 2300 - 2700 cm^{-1}. Even when the

salts are formed at liquid nitrogen temperatures in Freon 113 absorptions due to hydrohalides can be seen in the IR spectra[63].

It was because of these difficulties that no further work was carried out by the author. It is felt however, that although the simple salts mentioned thusfar are mixtures, ^{13}C nmr analysis of these mixtures at low temperature could have produced some rewarding results.

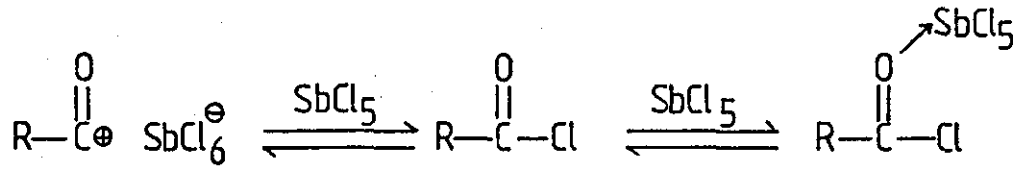
2.2.5 Reaction of acyl chlorides with amines in the presence of a Lewis acid

The reaction of benzoyl chloride with trimethylamine or triethylamine in the presence of antimony pentachloride at -78°C is known to give a salt of the type (30) shown below[14]:



(30) R'=Me,Et.

This is presumably formed via intermediates (31) or (32), complexes between the acyl chloride and antimony pentachloride.



(31) (32) R=Ph,alkyl.

With benzoyl chloride Olah[64] has shown that the complex (32) is the predominant species, i.e. it is a polarised donor-acceptor complex. With acetyl chloride, however, the complex (31) is predominant and it is essentially the acetylium salt that is present[64]. Both of these complexes have been isolated[65] and fully characterised using IR and nmr techniques[64].

This reaction route is also supported by the fact that when acetyl hexachloroantimonate is treated with triethylamine at -78°C, the expected

salt is not isolated[14]. The products formed are ketene and triethylammonium tetrachloroantimonate, by proton abstraction from the acetylium ion by the base. This reaction cannot take place when benzoyl chloride is used in place of acetyl chloride. These reactions are discussed further in the following sections.

We have seen that N-acyl-N,N,N-trialkylammonium chlorides can be formed at low temperatures in ether (section 2.2.4). The chloride ion can be replaced by the less nucleophilic tetrafluoroborate ion by reacting the salt with a 1:1 mixture of $HF:BF_3$ in ether at -78°C[13]. This reaction does not seem to be universally applicable as with benzoyl chloride and triethylamine and several other combinations, only ammonium salts were isolated. The same problem also occurs when hindered amines such as tri-n-butylamine or N,N-dimethyl-tert-butylamine are used. The salts formed are often stable at room temperature in the absence of moisture, and have been characterised using IR and ^1H nmr techniques.

All the salts mentioned above are known to be extremely hygroscopic and great care must be taken to exclude all moisture during reactions. The experimental techniques used in our work are discussed fully in the experimental section.

Our results are discussed below.

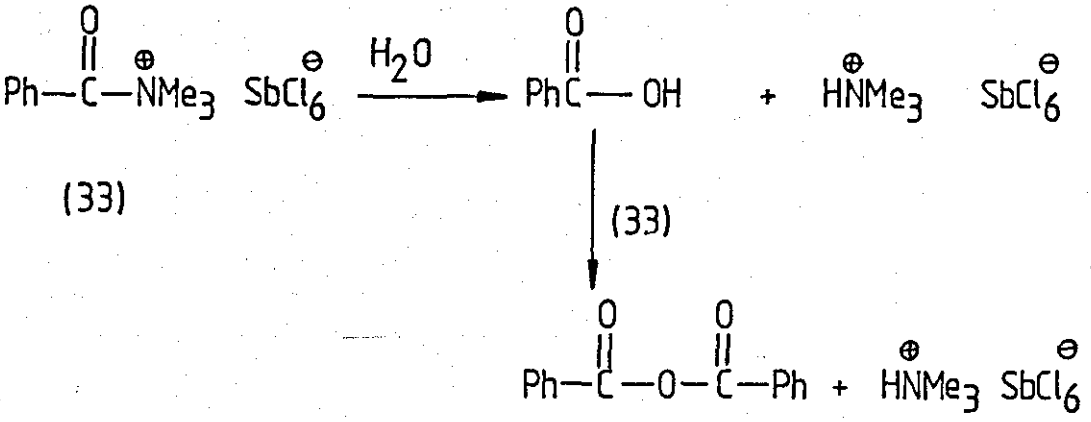
2.2.5.1 Reaction of benzoyl chloride with trimethylamine in the presence of antimony pentachloride

Reaction of benzoyl chloride with trimethylamine in the presence of antimony pentachloride according to the method of Klages[14] did not yield the expected N-benzoyl-N,N,N-trimethylammonium hexachloroantimonate as an isolable product.

Two solid products were isolated, namely, benzoic anhydride and trimethylammonium hexachloroantimonate. These were identified by comparison of the observed spectral data with those of authentic samples. The infrared spectrum showed no evidence for the presence of the expected salt, there being no peak in the 1800-1825 cm^{-1} region

which would be expected for this type of salt[13,63].

This result can be explained by hydrolysis of the salt (33) to give benzoic acid, which then reacts with a further molecule of (33) to give benzoic anhydride and trimethylammonium hexachloroantimonate.



Although benzoic anhydride was detected as one of the solid products from this reaction, its solubility in dichloromethane precluded its quantitative isolation. The dichloromethane washings were not analysed.

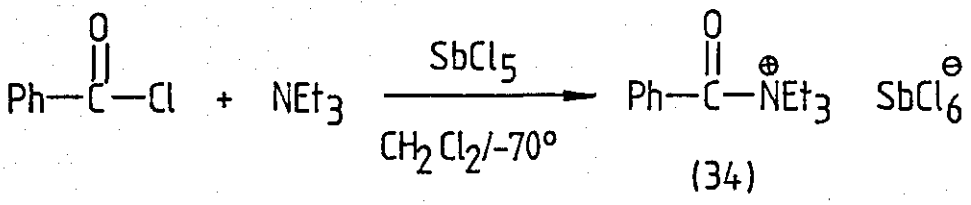
Anhydrides can be readily prepared by the reaction between an acyl chloride and an acid salt (from a free acid and a tertiary amine). Benzoic acid could be formed by hydrolysis of benzoyl chloride or the salt (33). Benzoyl chloride is unlikely to hydrolyse under these reaction conditions, as any water present would almost certainly react preferentially with antimony pentachloride to give a hydrate ($SbCl_5.H_2O$). It is known that benzoyl chloride and trimethylamine do not react together unless a Lewis acid is present[66]. The compound (33) is known to hydrolyse rapidly in the presence of water to give benzoic acid[14].

As the solid product is formed in high overall yield and the trimethylammonium salt is present in large quantities, it can be deduced that the salt (33) is indeed formed, is hydrolysed, and then reacts further to give the observed products.

The salt (33) has been prepared in low yield by the alkylation of N,N-dimethylbenzamide using trimethyloxonium tetrafluoroborate. The ^{13}C nmr spectrum is described in section 2.2.8.3.

2.2.5.2 Reaction of benzoyl chloride with triethylamine in the presence of antimony pentachloride

Reaction according to a modified method of Klages[14] gave a solid product which contained the expected product (34). Also formed were triethylammonium hexachloroantimonate and benzoic acid,



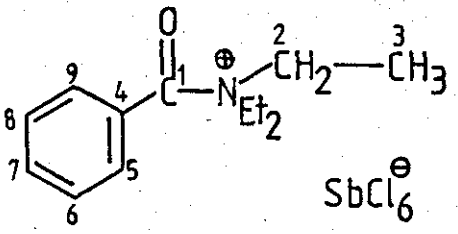
(34)

which were identified by comparison with authentic spectra (formed by hydrolysis of (34)).

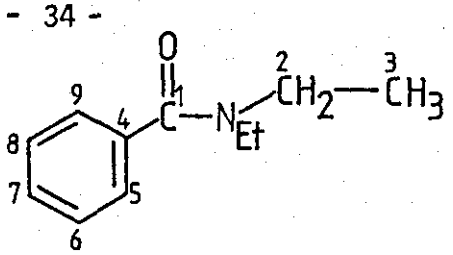
The infrared spectrum showed a strong peak at 1809 cm^{-1}, which is the carbonyl stretching frequency of (34). This is in close agreement with values given for other acylammonium salts that have been isolated in the past[13,63] i.e. 1800-1825 cm^{-1}. This high value compared with that for the amide (1631 cm^{-1}) reflects the loss of the mesomeric effect of the nitrogen in the acylammonium salt - the carbonyl stretching frequency moves to considerably higher frequency in these salts. A carbonyl stretching frequency was seen at 1695 cm^{-1}, which was due to benzoic acid. The two frequencies at 1795 and 1785 cm^{-1} cannot be explained - they are not due to the benzoyl chloride:antimony pentachloride adduct, which has peaks at 1656 and 1575 cm^{-} [64].

The products were analysed using ^{13}C nmr techniques.

Several important differences can be seen between (34) and (35). The methylene carbon in (34) has moved to lower field compared with that in (35), whereas the methyl carbon has moved to slightly higher field. This effect is also seen when comparing triethyloxonium salts with diethyl ether. The chemical shift of the carbonyl carbon has not changed significantly. However the chemical shifts of the aromatic carbons have changed. The quaternary aromatic carbon is most affected with an upfield shift of 9.9 ppm. The ortho-, meta- and para-carbons have been shifted downfield by 9.7 ppm, 1.1 ppm and



(34)



(35)

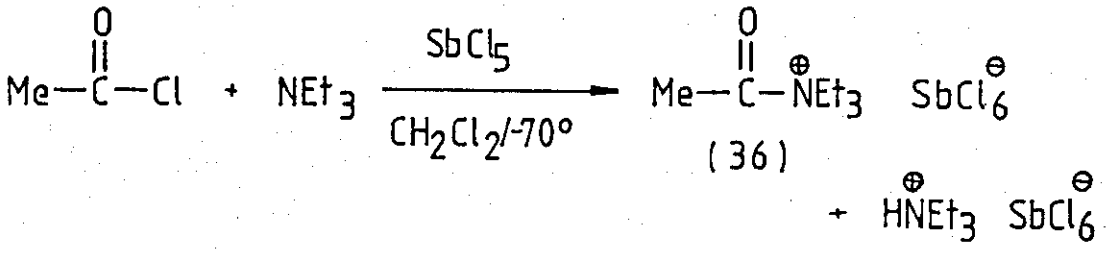
1.	172.0 ppm	6.	129.6	1.	171.3 ppm	6.	128.5
2.	52.9	7.	130.5	2.	43.5 (broad)	7.	129.1
3.	8.5	8.	129.6	3.	13.5 (broad)	8.	128.5
4.	127.6	9.	136.2	4.	137.5	9.	126.4
5.	136.2			5.	126.4		

1.4 ppm respectively. This sort of behaviour is also reported in section 2.2.8, later, when N,N-dialkylamides are O-alkylated using trialkyloxonium salts. This indicates that the benzoyl group is able to stabilise the positive charge on the nitrogen atom quite considerably c.f. N-phenoxycarbonyl-N,N,N-triethylammonium tetrafluoroborate. This is also supported by the fact that the chemical shifts of the methylene and methyl groups correspond closely to the values for tetramethylammonium salts, where the charge is spread over four ethyl groups ($Et_4\overset{+}{N}Br^-$ - 51.9, 7.4 ppm[51]).

It should be noted that although benzoic acid was formed in this reaction, it did not attack the salt (34) to give benzoic anhydride as seen in section 2.2.5.1. This is because the reaction was carried out at lower temperatures (-70°C vs. -30°C) and with a much reduced reaction time (4 hours vs. 1 week).

2.2.5.3 Reaction of acetyl chloride with triethylamine in the presence of antimony pentachloride

This reaction was carried out using the same procedure as that in section 2.3.5.2, and gave a solid product in 60% yield. This appeared to be a mixture of triethylammonium hexachloroantimonate and the expected product (36), which were identified by comparison with



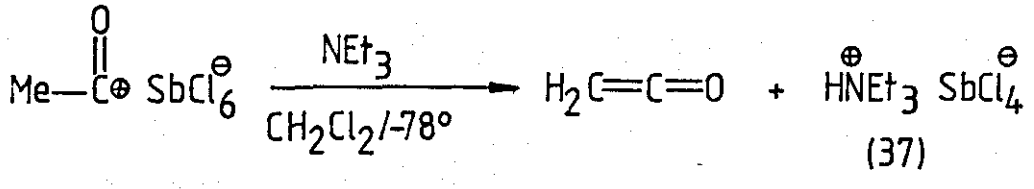
authentic spectra of the triethylammonium salt and N-acetyl-N,N,N-triethylammonium tetrafluoroborate[13] respectively.

Infrared analysis of the product showed a weak peak at 1822 cm^{-1}, which is assigned to the carbonyl stretching frequency of (36). This compares with a value of 1814 cm^{-1} for the tetrafluoroborate salt isolated by Paukstelis[13]. It should be noted that the complex between acetyl chloride and antimony pentachloride is essentially acetyl hexachloroantimonate and has peaks at 2283 cm^{-1} (v.s.), 1709 cm^{-1} (m) and 1587 cm^{-1} (w)[64]. Acetyl chloride itself exhibits a very strong peak at 1800 cm^{-1}.

Proton nmr measurements on the products showed the presence of quaternary amine salts, but there was no direct evidence for the presence of (36). This was verified by comparison of the spectral data of the product with that of the known salt isolated by Paukstelis[13].

^{13}C Nmr spectroscopy verified the presence of the triethylammonium salt, and also showed two small peaks at 50.8 and 7.5 ppm. These were possibly due to the presence of (36), being the chemical shifts for the methlyene and methyl groups attached to the nitrogen atom respectively. No other peaks were seen.

Klages has reported that the reaction of acetyl hexachloroantimonate with triethylamine did not give the expected product (36), but gave ketene and triethylammonium tetrachloroantimonate[14].



+ other products.

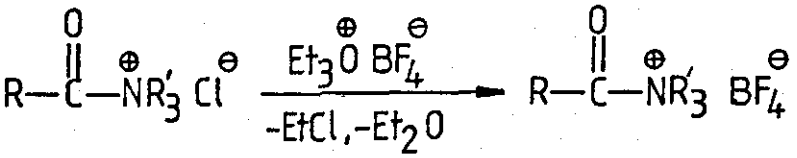
These were formed by abstraction of a proton from the acetylium ion by triethylamine and a reduction of the hexachloroantimonate ion to the tetrachloroantimonate ion. The compound (37) was prepared by another route and found to have a melting point of 92-94°C, c.f. our product mpt 192-194°C.

However, in our reaction the salt was initially formed at low temperature with the chloride ion as the counter-ion, and antimony pentachloride was added to the preformed salt. Compound (36) is also known to be unstable and breaks down to ketene and the triethylammonium salt (37) at higher temperatures[14]. It is postulated that our products were formed from the hydrolysis of (36) rather than by the breakdown described above. This is supported by the fact that our product had a high melting point, much higher than that of the tetrachloroantimonate salt. No value for the melting point of triethylammonium hexachloroantimonate has been reported.

2.2.6 Reaction of acyl chlorides with amines in the presence of triethyloxonium tetrafluoroborate

The reaction of acyl chlorides with amines at low temperatures has been discussed in section 2.2.4.

Paukstelis[13] has reported that the chloride ion in such salts can be exchanged for the relatively non-nucleophilic tetrafluoroborate ion by reaction with triethyloxonium tetrafluoroborate at -78°C:

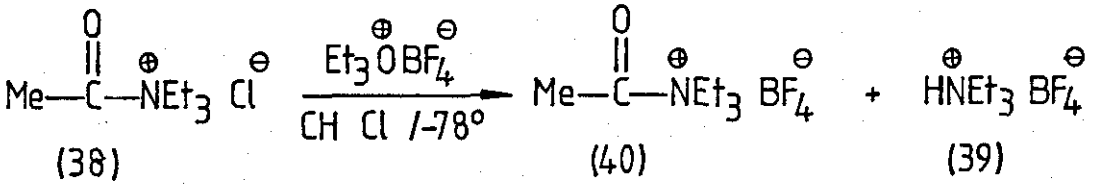


This reaction has limited scope. Reactions involving triethylamine, N-ethylpiperidine and pyridine give mixtures containing the hydrohalide salts. The isolable salts are stable under ether or as solids in a dry atmosphere at room temperature.

Our work is discussed in more detail below. It is felt that this area of work could have yielded some useful results if the experimental difficulties of excluding all moisture could have been overcome.

2.2.6.1 Reaction of acetyl chloride with triethylamine in the presence of triethyloxonium tetrafluoroborate

This reaction gave an unstable product which decomposed to an intractable tar. No spectra were obtained before decomposition. This result is surprising as Paukstelis has reported that the products were the expected salt (40) and the amine salt (39):



(38) (40) (39)

+ other products.

Our result may be attributable to moisture entering the system and reacting with the salt (40) to give acetic acid and the salt (39), although this has not been verified. The low yield may also be explained by the decomposition of (38) in solution before it reacts with the oxonium salt. This decomposition has been observed by Wedekind[62], who identified the products as ketene and triethylammonium chloride.

No further work was attempted in this area.

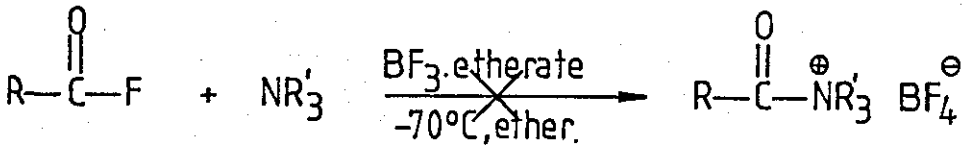
2.2.7 Reaction of acyl fluorides with amines in the presence of boron trifluoride etherate

There are no reports of such reactions in the literature.

It is known however, that acyl fluorides form complexes with

boron trifluoride in much the same way as acyl chlorides do with antimony pentachloride. These complexes are much less stable than the acyl chloride/antimony pentachloride complexes, and decompose above 20°C, e.g. acetyl fluoride/boron trifluoride complex decomposes at 20°C[67], and the benzoyl fluoride/boron trifluoride complex decomposes at -30°C[64].

It was felt that the reaction of acyl fluorides with amines at low temperatures in the presence of boron trifluoride etherate might provide a simple route to N-acylammonium salts (equation 3).



(equation 3)

In fact this was found not to be so as only dark brown tars were formed which proved to be complicated mixtures of products.

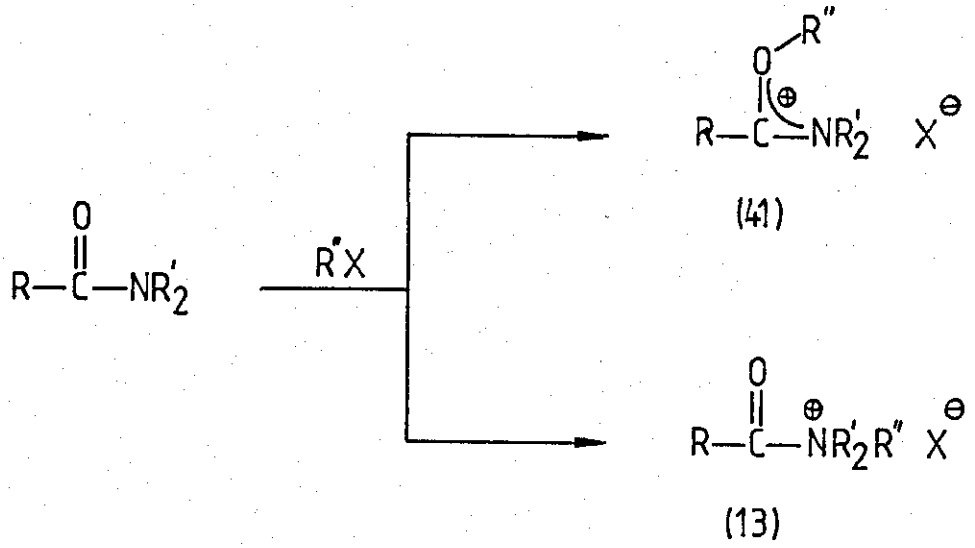
No further work was carried out.

2.2.8 Reaction of N,N-dialkylamides with alkylating agents

The alkylation reactions of amides have been widely studied and are discussed in some detail in a review by Challis[68]. Alkylation can take place in neutral, acidic or basic media, but it is the first that is of interest here. The amide is present in its unionised form and, because of its weak basicity, reacts slowly with alkylating agents. Only alkylating agents such as alkyl sulphates[69,70,71], oxonium salts[72,73] alkyl fluorosulphates[74,75] dialkylhalonium salts[75] and dialkoxycarbenium salts[75] are useful synthetically.

Our discussion from now on will be limited to N,N-dialkylamides i.e. tertiary amides.

There are two possible sites for alkylation, that is, on the nitrogen atom and/or on the oxygen atom. Both have been reported, the proportion of N- and O-alkylation products depending on the reaction temperature and reactivity of the alkylating agent.



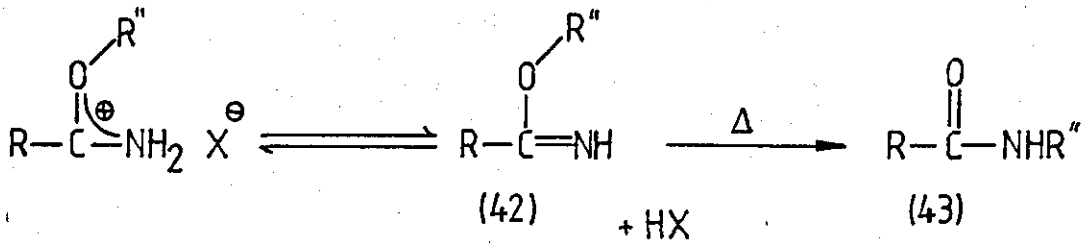
(41)

(13)

where $R''X$ = e.g. $MeOSO_2F$

In general, "low" temperature reactions favour O-alkylation (41) and "high" temperature reactions (> 60°C) favour N-alkylation (13). This temperature dependence suggests that O-alkylation occurs under kinetic control.

Close scrutiny of the intermediates and products (41) and (13) also supports this view. The energy of the transition state leading to the O-alkylation product (41) is lowered by the charge being delocalised over most of the molecule. Such delocalisation is not possible in the N-alkylation product (13) where the induced charge is localised on the nitrogen atom, and the transition state energy is therefore higher (thermodynamic control). It is also known that O-alkyl imidates (42) can rearrange to the corresponding N-alkylamide (43) on heating. This reaction is known as the Chapman rearrangement[76].

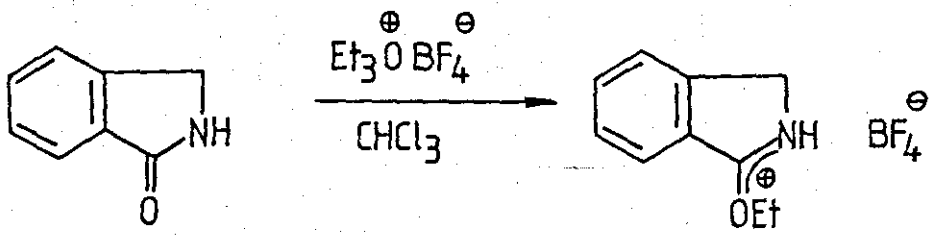


(42) + HX (43)

With tertiary amides the corresponding O-alkylamidonium salt cannot lose a proton in the way shown above, and a comparable O to N rearrangement will only occur if the displaced N-alkyl substituent forms a

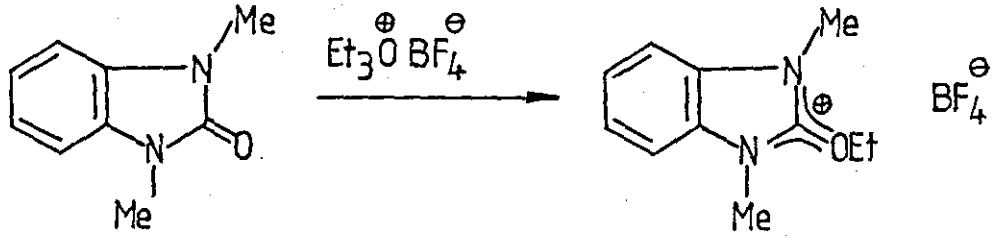
relatively stable carbenium ion.

There are many examples of alkylation of tertiary amides and lactams using strong alkylating agents such as triethyloxonium tetrafluoroborate and methyl fluorosulphate. Peterson[72] reported that phthalimidines (44) are alkylated solely on the oxygen atom when triethyloxonium tetrafluoroborate is used. Meerwein[78] reported that



(44)

alkylation of 1,3-dimethyl-2-imidazolidinone with triethyloxonium tetrafluoroborate gives an O-alkylated product in 47% yield and an N-alkylated product in 41% yield. However when 1,3-dimehtyl-2-benzimidazolidinone(45)is alkylated under similar conditions, only the O-alkylated product is seen. This is presumably because there is severe steric hinderance for attack at the nitrogen atom.

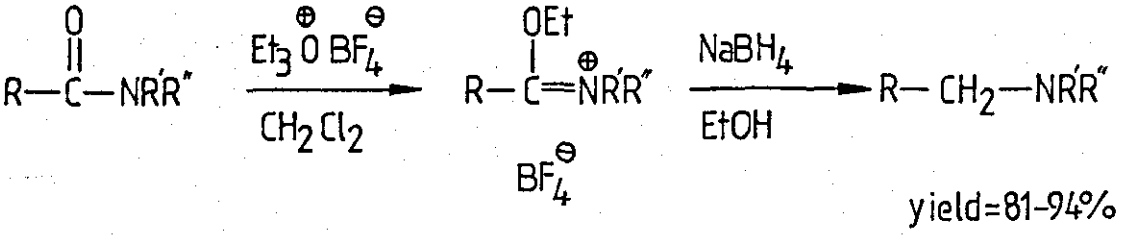


(45) 97% yield.

Alkylation of N,N-dimethylacetamide with either triethyloxonium tetrafluoroborate[73] or methyl/ethyl fluorosulphates[74] gives the O-alkylated product in high yields. With N,N-dimethylformamide, alkylation with triethyloxonium tetrafluoroborate yields only the O-alkylated product, whereas with the alkyl fluorosulphates, the major product is the O-alkylated product (95%) and the N-alkylated product is formed in low yield (c.a. 5%). A similar situation exists with tetramethylurea. Alkylation with trialkyloxonium salts yields only the O-alkylated product[73]. When alkyl fluorosulphates are used the

N-alkylated product is also formed in about 5% yield[74]. This difference in selectivity reflects the relative reactivities of the alkylating agents.

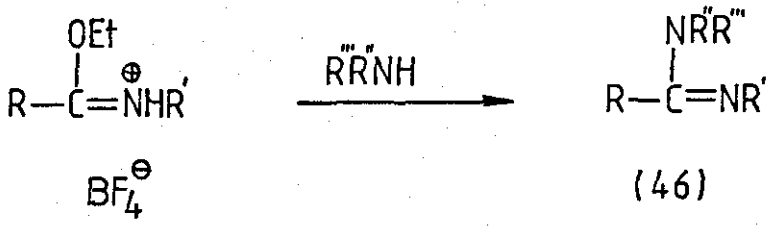
This type of reaction has been used in many synthetic applications. Borch has developed a method of reducing secondary and tertiary amides using triethyloxonium tetrafluoroborate[77] (equation 4):



yield=81-94%

(equation 4)

Amidines (46) have been prepared by reacting amines with O-alkyl-amidonium (imidate) salts that have been prepared by alkylation of primary and secondary amides with triethyloxonium tetrafluoroborate[78] (equation 5):



(46)

(equation 5)

Hydrolysis of these O-alkylamidonium salts has also been used as a method for cleaving amides between the carbonyl group and the nitrogen atom[79].

There seems to have been little work done on these alkylating salts using nmr techniques[74,75], and no work has been reported using ^{13}C nmr spectroscopy.

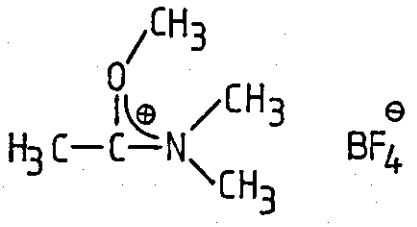
The following section describes the work we have done in this area. We have investigated the reactions of several simple N,N-dialkyl amides with either trimethyl- or triethyloxonium tetrafluoroborate, and have analysed their ^{13}C nmr spectra.

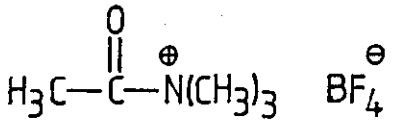
The reactions were carried out in nmr tubes sealed with a rubber septum so that moisture was excluded. The salts were not isolated as such but were formed in solution (usually d_2-dichloromethane), and their ^{13}C nmr spectra were recorded generally at room temperature.

The results are given in tables 2 and 3 below. Table 2 shows the results using trimethyloxonium tetrafluoroborate as the alkylating agent, and table 3 those with triethyloxonium tetrafluoroborate.

2.2.8.1 Alkylation of N,N-dimethylacetamide

Methylation using trimethyloxonium tetrafluoroborate gave the results shown in table 2. The ^{13}C nmr spectrum shows the presence of two products after 24 hours at room temperature. The reaction goes to completion.

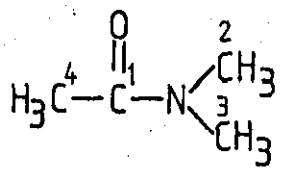
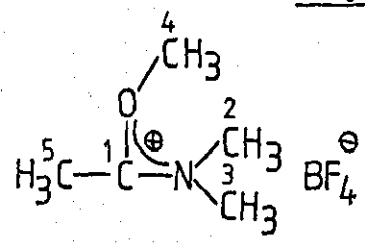
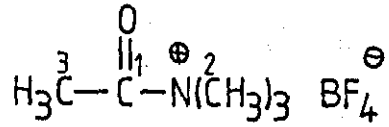
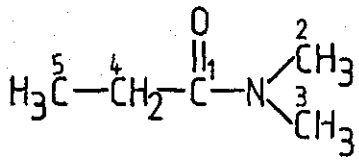
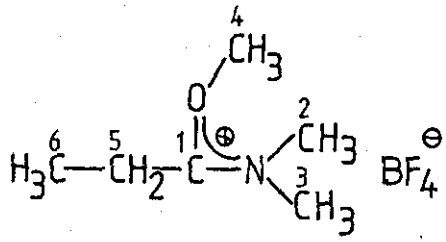
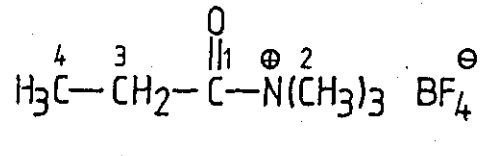




The major product is the expected O-alkylated product. The two methyl groups attached to the nitrogen atom have moved downfield by 4.2 ppm and 4.7 ppm respectively when compared with the starting material. It can be seen that the positive charge is stabilised over the O-, C- and N-atoms as shown. This is supported by the fact that the methyl carbons in trimethyloxonium tetrafluoroborate have a ^{13}C nmr shift of 78.8 ppm[80], and those in tetramethylammonium chloride have a ^{13}C nmr shift of 56.2 ppm[81], i.e. they are at much lower field when only one hetero-atom is involved. The methyl carbon in the acetyl- group was also seen to move 6.3 ppm to higher field which would be expected for this structure. The carbonyl carbon shifted from 169.5 ppm in the amide to 176.9 ppm in the major product which again reflects the stabilisation of the positive charge.

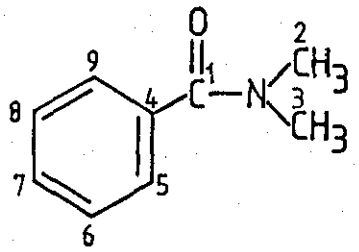
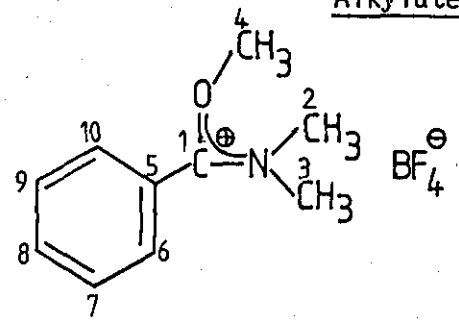
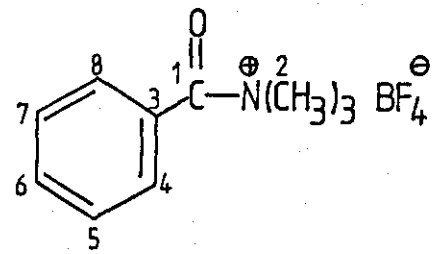
The minor product appears to be the N-alkylated product, which is surprising as Alder[74] has reported that no N-alkylation occurs when the

Table 2

Amide	Conditions[a]	Alkylated Products		
1. 	CD_2Cl_2, r.t.; $Me_3O^{\oplus}\ BF_4^{\ominus}$			
1. 169.5ppm	3. 34.0	1. 176.9ppm	4. 60.5	1. 174.6ppm 3. 18.0
2. 37.0	4. 20.4	2. 41.2	5. 14.1	2. 57.8
		3. 38.7		
2. 	CD_2Cl_2, r.t.; $Me_3O^{\oplus}\ BF_4^{\ominus}$			
1. 172.9ppm	4. 25.7	1. 179.5ppm	4. 60.3	1. 178.1ppm 3. 25.0
2. 36.2	5. 8.4	2. 40.7	5. 20.6	2. 57.7 4. 8.4
3. 34.4		3. 38.9	6. 8.1	

(a) See experimental for full details

Table 2 cont.

Amide	Conditions[a]	Alkylated Products	
3. 	CD_2Cl_2, r.t. $Me_3O^{\oplus}\ BF_4^{\ominus}$		

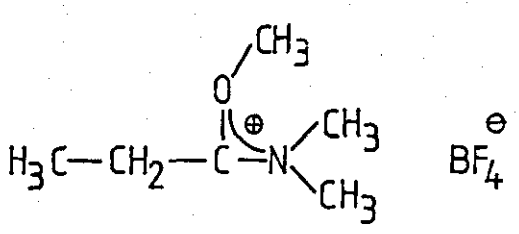
1.	171.3 ppm	6.	128.3	1.	174.3 ppm	6.	not assigned	1.	173.7 ppm	5.	not assigned
2.	40.0	7.	129.5	2.	42.4	7.	"	2.	59.4	6.	"
3.	36.8	8.	128.3	3.	38.8	8.	"	3.	not assigned	7.	"
4.	136.6	9.	127.1	4.	62.4	9.	"	4.	"	8.	"
5.	127.1			5.	not assigned	10.	"				

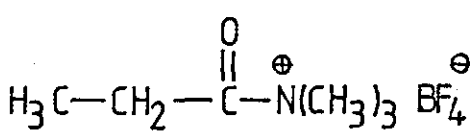
(a) See experimental for full details

amide is treated with ethyl or methyl fluorosulphonates. The carbonyl carbon has moved downfield by 5.1 ppm which might be expected for this type of product. The methyl carbon in the acetyl group moved upfield slightly (2.4 ppm) which again supports this structure. The methyl carbons attached to the nitrogen atom have moved downfield to give a single peak at 57.8 ppm. When compared with that of the carbons in tetramethylammonium chloride (56.2 ppm), where the positive charge is stabilised by four methyl groups, this shift of 57.8 ppm supports the structure shown, where the positive charge is stabilised by three methyl groups.

2.2.8.2 Alkylation of N,N-dimethylpropionamide

The amide was methylated using trimethyloxonium tetrafluoroborate to give the results shown in table 2. The ^{13}C nmr spectrum shows two products to be present after 24 hours at room temperature. The reaction goes to completion.





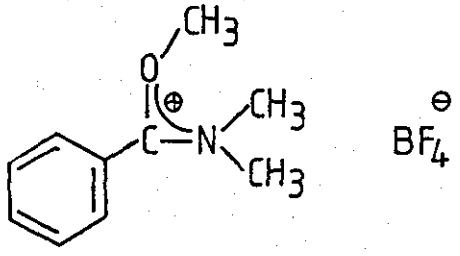
The major product is the O-alkylated amide as expected. The positive charge was stabilised over the O-, C- and N-atoms. This is supported by the chemical shifts of the groups attached to these atoms. As in section 2.2.8.1, the chemical shift of the methyl carbons attached to the nitrogen atom (40.7/38.9 ppm) indicates that, although the nitrogen atom is helping to stabilise the positive charge, it is not stabilised solely by this atom. This argument also applies to the methyl group on the oxygen atom (60.3 ppm). The methylene carbon of the propionyl group has moved from 25.7 ppm in the amide to 20.6 ppm in the O-alkylated product, which reflects the stabilisation of the positive charge. This is also noticed to a lesser extent in the upfield shift of 0.3 ppm of the methyl carbon in this group. The carbonyl carbon has moved downfield by 6.6 ppm to 179.5 ppm in the

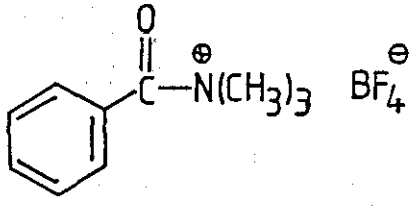
alkylated product, which is similar to that seen in section 2.2.8.1.

The minor product is the N-alkylated product. The carbonyl carbon has moved from 172.9 ppm in the amide to 178.1 ppm in the product, a downfield shift of 5.2 ppm. This compares well with that seen in section 2.2.8.1, and reflects the presence of the positively charged nitrogen atom next to it. The methylene carbon has only been slightly affected by the presence of the positively charged nitrogen, showing an upfield shift of 0.7 ppm. The methyl carbon next to this group has not moved at all. The methyl carbons attached to the positively charged nitrogen show a single peak at 57.7 ppm which again supports the structure shown.

2.2.8.3 Alkylation of N,N-dimethylbenzamide

Methylation using trimethyloxonium tetrafluoroborate gave the results shown in table 2. ^{13}C Nmr shows the presence of two products after 24 hours at room temperature. The reaction goes to completion.





The major product is the expected O-alkylated product. Again the positive charge was seen to be stabilised over the O-, C- and N-atoms. The two methyl carbons attached to the nitrogen atom have moved from 40.0 ppm and 36.8 ppm in the amide to 42.4 ppm and 38.8 ppm, downfield shifts of 2.4 ppm and 2.0 ppm respectively. Comparison of these values with that of the methyl carbon in tetramethylammonium chloride (56.2 ppm) show that the positive charge is not based solely on the nitrogen atom. Indeed, comparison of the change in shift of these methyl carbons with the changes seen in section 2.2.8.1 (4.2 ppm and 4.7 ppm) and section 2.2.8.2 (both 4.5 ppm) indicates that the aromatic

ring is affecting the way the positive charge is being stabilised. This would be noticeable in the ^{13}C nmr shifts of the aromatic carbons, but unfortunately no assignments could be made for these because of the complications arising from having another product present, viz. the N-alkylated product. An example where aromatic assignments could be made is given in 2.2.8.6.

This change in stabilisation is also evident from the slight change in chemical shift of the methyl carbon attached to the oxygen atom - 62.4 ppm in this example compared with ca. 60.4 ppm in previous examples.

The carbonyl carbon has moved downfield by 3.0 ppm compared with the amide. This shift is smaller than that seen in sections 2.2.8.1 and 2.2.8.2 where shifts of 7.4 ppm and 6.6 ppm were seen, respectively, which suggests that the aromatic ring is making a significant contribution to the stabilisation of the system.

The minor product is the N-alkylated product. The carbonyl carbon shows a peak at 173.7 ppm, a downfield shift of 2.4 ppm when compared with the amide. This compares well with the value for the triethyl-salt described in section 2.2.5.2. The methyl carbons show a single peak at approximately 59.4 ppm. The aromatic carbons could not be assigned owing to the complexity of the spectrum in this region. Attempts to prepare this salt by another route proved to be unsuccessful (see section 2.2.5.1).

2.2.8.4 Alkylation of N,N-diethylacetamide

Ethylation using triethyloxonium tetrafluoroborate gave the results shown in table 3. The ^{13}C nmr spectrum shows a single alkylated product after 24 hours at room temperature. The reaction goes to completion.

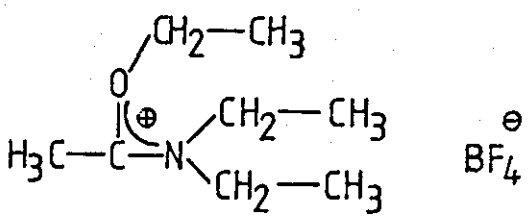
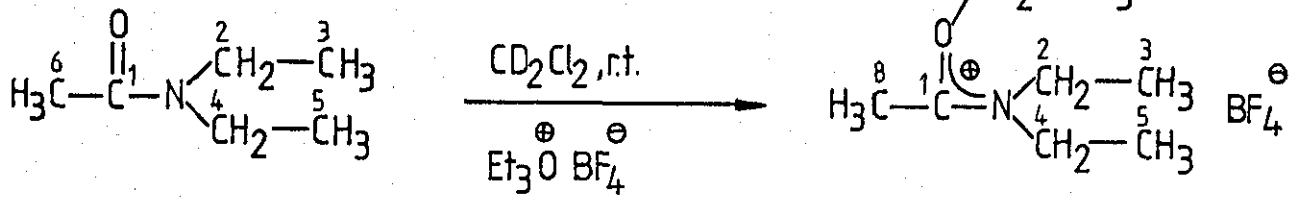


Table 3

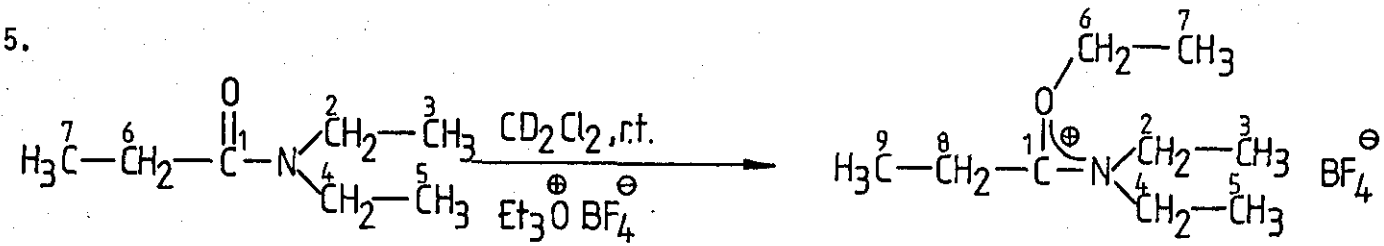
Amide	Conditions[a]	Alkylated Products

4.



1. 168.6 ppm	4. 38.9		1. 175.8 ppm	4. 45.5	7. 11.5
2. 41.9	5. 12.1		2. 47.4	5. 12.2	8. 14.6
3. 13.2	6. 20.3		3. 13.9	6. 71.0	

5.



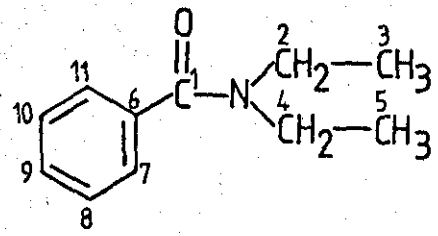
1. 171.8 ppm	5. 12.1		1. 178.7 ppm	4. 45.3	7. 11.7
2. 40.9	6. 25.2		2. 47.0	5. 12.8	8. 21.1
3. 13.3	7. 8.6		3. 14.1	6. 70.8	9. 9.4
4. 39.1					

(a) See experimental for full details.

Table 3 cont.

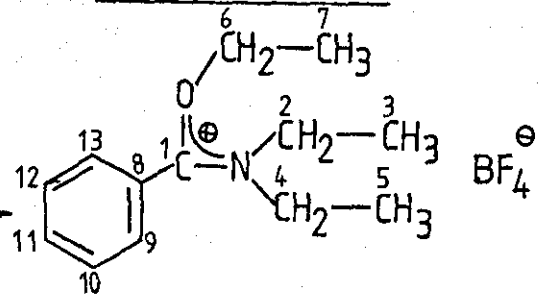
Amide	Conditions[a]	Alkylated Products

6.



CD_2Cl_2, r.t.

$Et_3O^{\oplus}\ BF_4^{\ominus}$



1.	171.3 ppm	7.	126.4		
2.	43.5	8.	128.5		
3.	13.5	9.	129.1		
4.	43.5	10.	128.5		
5.	13.5	11.	126.4		
6.	137.5				

1.	174.3 ppm	6.	73.3	11.	133.2
2.	48.3	7.	11.7	12.	127.4
3.	14.1	8.	124.8	13.	130.0
4.	45.2	9.	130.0		
5.	12.6	10.	127.4		

as above

SO_2/CD_2Cl_2, -25°C

$Et_3O^{\oplus}\ BF_4^{\ominus}$

as above

1.	174.2 ppm	6.	73.7	11.	133.6
2.	48.4	7.	11.7	12.	127.2
3.	14.4	8.	124.5	13.	130.6
4.	45.2	9.	130.6		
5.	12.8	10.	127.2		

Reaction did not go to completion - starting material still present after 5 days

(a) See experimental for full details.

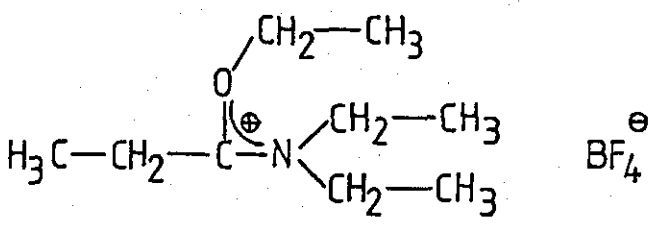
This product was identified as the O-alkylated product, as expected. The positive charge is stabilised as in previous examples i.e. over the O-, C- and N- atoms. This is supported by the change in chemical shift of the methylene carbons attached to the nitrogen. In the amide these are at 40.9 ppm and 39.1 ppm, whereas in the product they are at 47.0 ppm and 45.3 ppm, a downfield shift of 6.1 ppm and 6.2 ppm respectively. A similar, though less pronounced, shift is seen in the methyl carbons (shifted downfield by 0.8 ppm and 0.7 ppm respectively). The methylene carbon next to the oxygen atom in the product showed a chemical shift of 71.0 ppm which reflects the stabilisation of the positive charge over the three atoms. The methyl carbon in this group gives a peak at 11.5 ppm. These values should be compared with those for triethyloxonium tetrafluoroborate and tetraethylammonium iodide, where the positive charge is on one hetero-atom, and show peaks at 84.4 ppm/12.2 ppm[82] and 54.4 ppm/9.5 ppm[83] respectively.

The carbonyl carbon in the amide shows a peak at 168.6 ppm which on O-alkylation moves to 175.8 ppm, a downfield shift of 7.2 ppm. The methyl carbon of the acetyl group is also affected by the positive charge distribution in the alkylated product. The methyl carbon moves from 20.3 ppm in the amide to 14.6 ppm in the product, i.e. an upfield shift of 5.7 ppm. This type of shift would be expected for this product and is comparable with that seen in the methylation of N,N-dimethylacetamide (section 2.2.8.1).

There is no evidence for the formation of the N-alkylated product, even after a prolonged period. Diethyl ether was seen in the spectrum, formed as a by-product from the alkylation reaction of triethyloxonium tetrafluoroborate.

2.2.8.5 Alkylation of N,N-diethylpropionamide

The amide was ethylated using triethyloxonium tetrafluoroborate to give the results shown in table 3. ^{13}C Nmr shows the presence of a single alkylated product after 24 hours at room temperature. The reaction goes to completion.



The product was identified as the expected O-alkylated salt. The positive charge is stabilised in the usual manner, i.e. over the O-, C- and N- atoms. The methylene carbons of the ethyl groups attached to the nitrogen atom show downfield shifts of 6.1 ppm and 6.2 ppm, which are identical to those observed in section 2.2.8.4 above. A similar, smaller shift was seen in the methyl carbons of these groups, the shifts being 0.8 ppm and 0.7 ppm downfield from those in the amide.

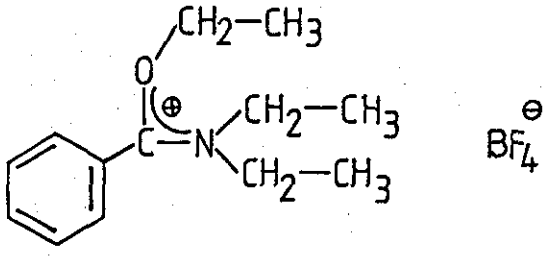
The methylene carbon of the O-ethyl group gives a peak at 70.8 ppm, and the methyl carbon is at 11.7 ppm. The methylene carbon of the propionyl group has moved upfield by 4.1 ppm compared with the amide, whilst the methyl carbon has moved downfield by 0.8 ppm. The carbonyl carbon in the amide shows a peak at 171.3 ppm, which has moved downfield by 6.9 ppm on O-alkylation.

There is no evidence for the formation of the N-alkylated product. Diethyl ether is again seen as a by-product of the alkylation reaction.

2.2.8.6 Alkylation of N,N-diethylbenzamide

The amide was ethylated using triethyloxonium tetrafluoroborate to give the results shown in table 3. Two reactions were carried out, one in d_2-methylene chloride at room temperature, and the other in sulphur dioxide at -25°C. The former goes to completion in 24 hours, whereas the latter is still incomplete after 5 days. The results are discussed in detail below.

(a) Reaction in d_2-methylene chloride

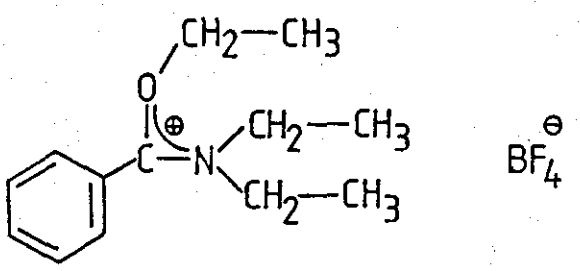


The methylene carbons of the ethyl groups attached to the nitrogen atom show downfield shifts of 4.8 ppm and 1.7 ppm respectively compared with the amide. However, this picture is rather misleading as the methylene carbons in the amide have been observed to give two peaks in the ^{13}C nmr spectrum under certain conditions[84]. If these are taken as 43.5 ppm and 39.4 ppm we obtain downfield shifts of 4.8 ppm and 5.8 ppm respectively. Similarly, for the methyl carbons we see a downfield shift of 1.1 ppm. This change of chemical shift is less pronounced than the examples in sections 2.2.8.4 and 2.2.8.5, and reflects the presence of the aromatic ring. This influence is also apparent when the chemical shifts of the methylene and methyl carbons of the O-ethyl group (73.3 ppm and 11.7 ppm) are compared with the previous two examples (approx. 71.0 ppm and 12.5 ppm). This seems to indicate that the positive charge is being stabilised more by the oxygen/aromatic side of the molecule than the nitrogen side. The carbonyl carbon has moved downfield by 3.0 ppm in the alkylated product compared with the amide. This is a much smaller shift than that seen in sections 2.2.8.4 and 2.2.8.5 and again reflects the stabilising influence of the aromatic ring.

Study of the aromatic carbon shift supports this hypothesis. The ortho- and para- carbons have moved downfield by 3.6 ppm and 4.1 ppm respectively, whereas the meta- and quaternary carbons have moved upfield by 1.1 ppm and 12.7 ppm respectively. These are similar to the chemical shifts one would expect to see with strongly electron withdrawing substituents such as a cyano-group attached to the aromatic ring.

There is no evidence of N-alkylation.

(b) Reaction in liquid sulphur dioxide



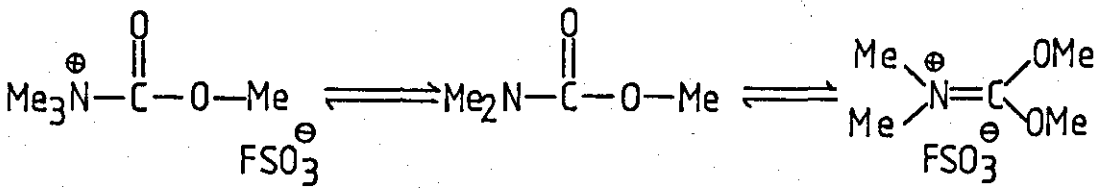
The reaction does not go to completion after 5 days at -25°C. The peaks for the O-alkylated product can be clearly seen in the ^{13}C nmr spectrum of the reaction mixture. There is no evidence of N-alkylation.

2.2.9 Reaction of N,N-dialkylcarbamates with alkylating agents

The alkylation of N,N-dialkylcarbamates using strong alkylating agents such as triethyloxonium tetrafluoroborate and alkyl fluorosulphates has been studied by Meerwein[73] and Alder[20] and has provided some interesting results.

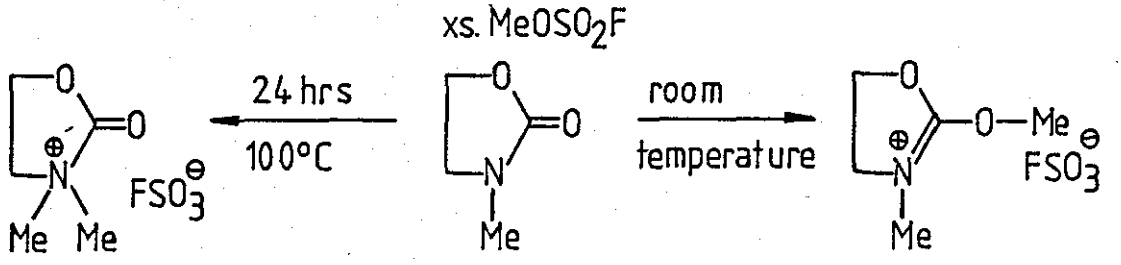
Meerwein found that alkylation of ethyl N,N-dimethylcarbamate gives only the O-alkylated (kinetic) product at room temperature, and in low yield (no figure quoted)[73].

Alder, however, has found that methylation of methyl N,N-dimethylcarbamate using methyl fluorosulphate gives predominantly the N-alkylated (thermodynamic) product at room temperature[20]. Initially the rate constants for O- and N-alkylation are very similar, but after 33.5 hours the solution contained 76% of the N-alkylated product (47), 11.5% of the O-alkylated product (48) and 12.5% of unchanged carbamate.



(47) (48)

Indeed it was found that the N-alkylation product was favoured by at least 99:1 at equilibrium. This contrasts with the fact that protonation of the carbamate in fluorosulphonic acid is >95% on the carbonyl oxygen which is normal for carbamates[101]. It was thought that this difference might be explained by the presence of an $A^{1,3}$ interaction between the two methyl groups in either planar conformation of (48). Because of this N-methyl-2-oxazolidone (49) was investigated under similar conditions. O-Alkylation takes place rapidly to give (51) and



(50) (49) (51)

virtually no (50) (< 5%), the reaction being complete in less than 1 minute. The rate of reaction of (49) is at least 1000 times that for the simple carbamate described initially. However, after 24 hours at 100°C (50) is formed and does not revert into (51) during 24 hours at 100°C (< 10% (51) formed). Again, the N-alkylated product is strongly favoured at equilibrium but protonation is greater than 95% on oxygen. Obviously the steric explanation is inadequate.

The HSAB theory points us in the right direction i.e. the softer acid favours the softer basic centre (nitrogen), but it is obviously important to distinguish between nucleophilicity and basicity towards cationic methylating agents.

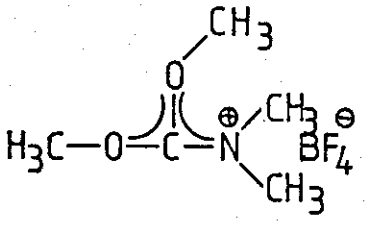
The following section describes the work we have done in this area using trialkyloxonium tetrafluoroborates and several simple N,N-dialkylcarbamates. The ^{13}C nmr spectra of the products are analysed and discussed in detail.

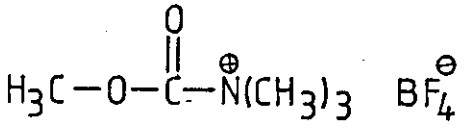
All reactions were carried out in nmr tubes sealed with a rubber septum to exclude moisture. The salts were not isolated, but were formed in d_2-dichloromethane solution at room temperature.

Our results are tabulated in Table 4 below.

2.2.9.1 Alkylation of methyl N,N-dimethylcarbamate

Methylation with trimethyloxonium tetrafluoroborate gave the results shown in table 4. ^{13}C Nmr spectroscopy showed the presence of two products and also that the reaction had not gone to completion.



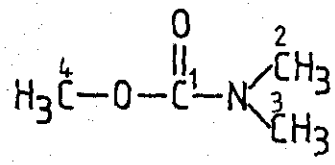
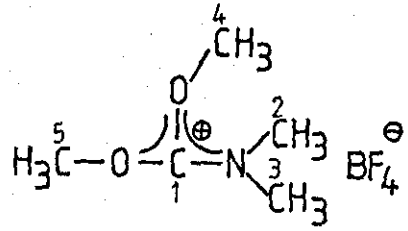
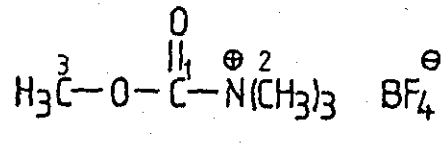
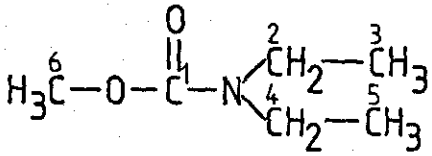
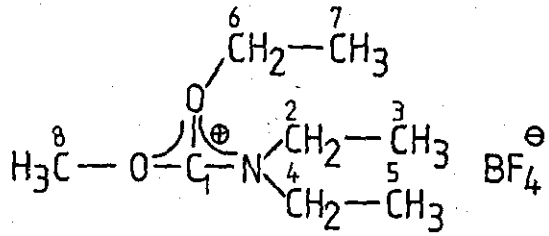


The major product is the O-alkylated material. This shows a single peak for the two N-methyl carbon atoms at 38.7 ppm, a downfield shift of 2.6 ppm compared with the carbamate. The carbonyl carbon shows little change in chemical shift in the O-alkylated product (a downfield shift of 0.8 ppm). The two O-methyl carbon atoms give a single peak at 62.6 ppm.

Comparison of the changes in chemical shifts seen in this example with those seen in N,N-dimethylacetamide (section 2.2.8.1) reflect a change in the stabilisation of the positive charge.

In the amide the N-methyl groups move downfield by 4.2 ppm and 4.7 ppm compared with 2.6 ppm in the carbamate. Also the O-methyl carbon in the amide is at 60.5 ppm compared with 62.6 ppm for the two O-methyl carbons in the carbamate. This suggests that the positive charge is stabilised by all three hetero-atoms in the carbamate compared with only two in the amide equivalent.

Table 4

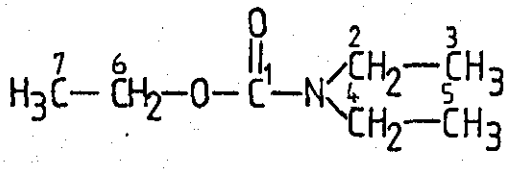
Carbamate	Conditions[a]	Alkylated Products	
1. 	SO_2/CD_2Cl_2, -20°C; $Me_3O^{\oplus}BF_4^{\ominus}$		
1. 157.3 ppm 3. 36.1 2. 36.1 4. 52.5		1. 158.1 ppm 4. 62.6 2. 38.7 5. 62.6 3. 38.7	1. 154.1 ppm 3. 59.0 2. 59.9
2. 	CD_2Cl_2, r.t.; $Et_3O^{\oplus}BF_4^{\ominus}$		Reaction did not go to completion.
1. 156.7 ppm 4. 41.6 2. 41.6 5. 13.8 3. 13.8 6. 52.2		1. 162.4 ppm 5. 14.6 2. 45.1 6. 74.4 3. 14.6 7. 12.0 4. 45.1 8. 62.4	

(a) See experimental for full details.

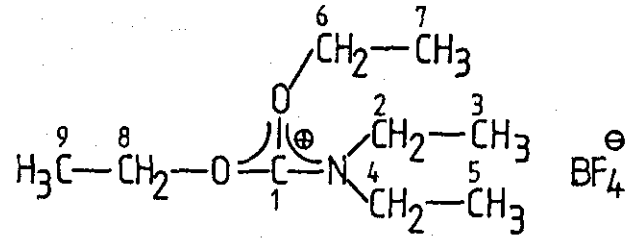
Table 4 cont.

Carbamate	Conditions[a]	Alkylated Products

3.

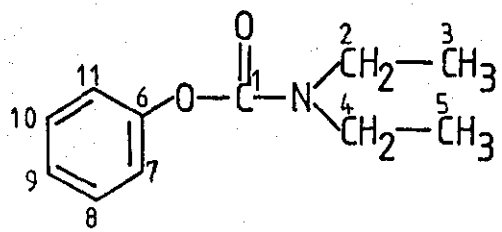


$\xrightarrow[Et_3O^{\oplus}\,BF_4^{\ominus}]{CD_2Cl_2,\ r.t.}$

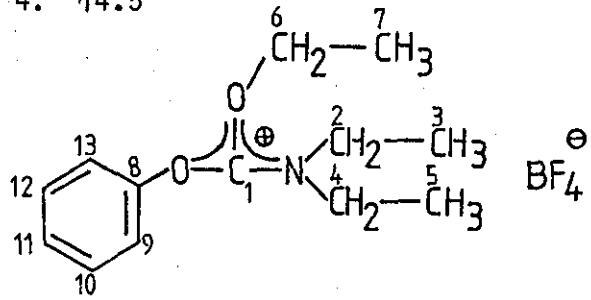


Reaction did not go to completion.

1. 156.0 ppm	5. 13.8	1. 161.8 ppm	6. 74.1
2. 41.6	6. 60.7	2. 45.1	7. 12.1
3. 13.8	7. 14.7	3. 14.5	8. 74.1
4. 41.6		4. 45.1	9. 12.1
		4. 14.5	



$\xrightarrow[Et_3O^{\oplus}\,BF_4^{\ominus}]{CD_2Cl_2,\ r.t.}$



Reaction did not go to completion.

1. 154.3 ppm	7. 121.9	1. 159.1 ppm	8. 152.0
2. 42.1	8. 129.2	2. 46.0	9. 117.9
3. 13.9	9. 125.1	3. 14.0	10. 131.3
4. 42.1	10. 129.2	4. 46.0	11. 127.6
5. 13.9	11. 121.9	5. 14.0	12. 131.3
6. 151.8		6. 74.4	13. 117.9
		7. 12.0	

(a) See experimental for full details.

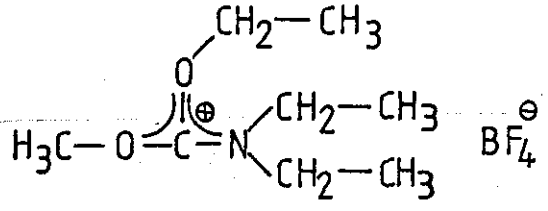
On prolonged storage at -25°C the amount of O-alkylated product increased.

The minor product is the expected N-alkylated product reported by Alder[74]. It shows a single peak at 59.9 ppm for the three methyl carbons attached to the positively charged nitrogen atom, a downfield shift of 23.8 ppm compared with the carbamate. The methyl carbon next to the oxygen atom gives a single peak at 59.0 ppm, a downfield shift of 6.5 ppm compared with the carbamate. The carbonyl carbon has moved upfield by 3.2 ppm to give a peak at 154.1 ppm in the product. This shift in the carbonyl carbon compared well with the example in section 2.2.3.1 (N-phenoxycarbonyl-N,N,N-triethylammonium tetrafluoroborate) where it moved from 154.3 ppm in the carbamate to 151.8 ppm in the ammonium salt, an upfield shift of 2.5 ppm. However, the yield was low and did not seem to increase on prolonged storage at -25°C.

This contrasts with the findings of Alder[20], who found that methylation of the carbamate with methyl fluorosulphonate at room temperature gave the N-alkylated form as the major product.

2.2.9.2 Alkylation of methyl N,N-diethylcarbamate

The carbamate was ethylated using triethyloxonium tetrafluoroborate. The results of ^{13}C nmr analysis of the products are shown in table 4. Although a single product was formed the reaction did not go to completion.

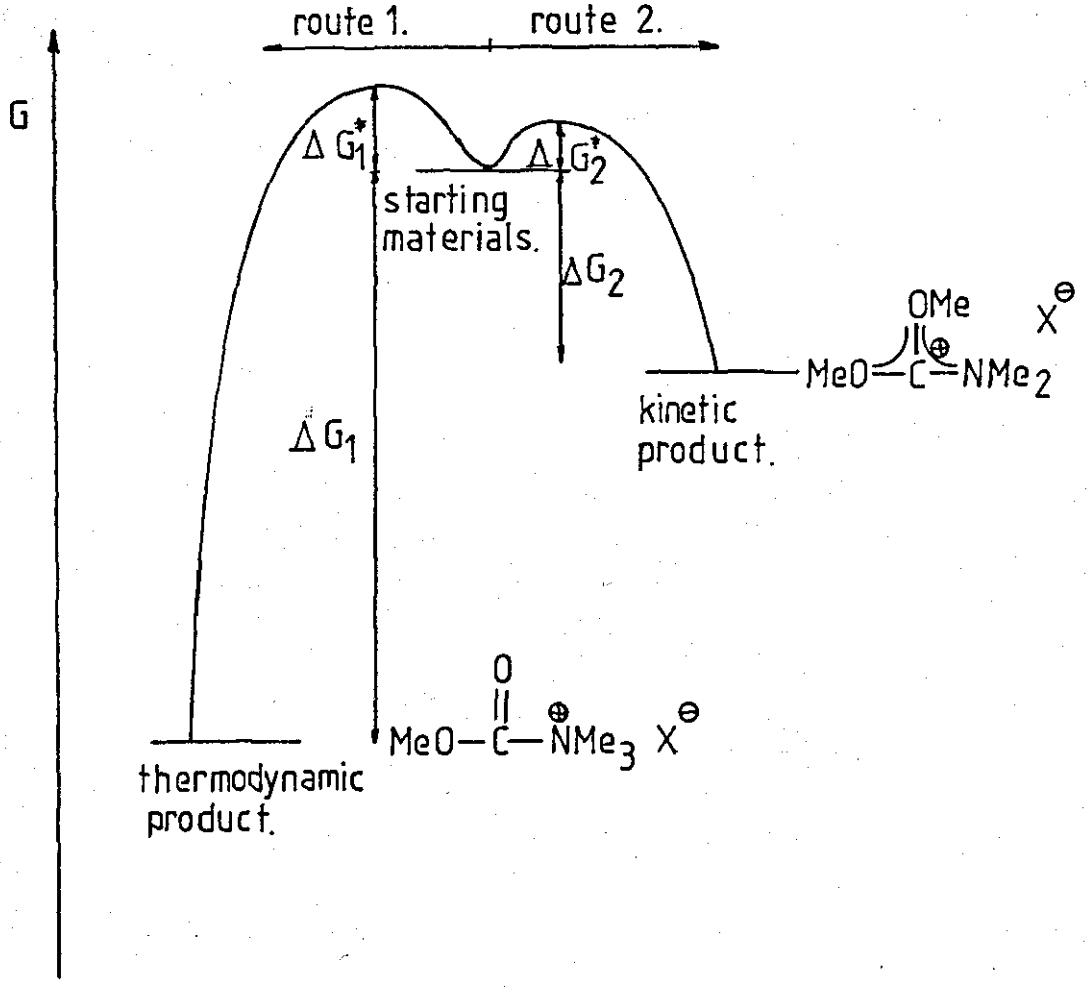


The product was identified as the O-alkylated material. The methylene carbons next to the nitrogen atom have moved downfield by 3.5 ppm in the product. The corresponding methyl carbons have also moved 0.8 ppm downfield. The methylene carbon next to the oxygen atom gives a peak at 74.4 ppm and the methyl carbon next to it a peak at

12.0 ppm. The methyl carbon next to the other oxygen atom gives a peak at 62.4 ppm. The carbonyl carbon has moved downfield by 5.7 ppm in the alkylated product.

The stabilisation of the positive charge over three hetero-atoms is again noticeable when these changes in chemical shifts are compared with those seen in the alkylation of the equivalent N,N-diethylacetamide, where it is spread over two hetero-atoms (section 2.2.8.4). In the carbamate the changes in chemical shift of the methylene and methyl carbons attached to the nitrogen atom are 3.5 ppm and 0.8 ppm respectively, compared with 6.1, 6.2 ppm and 0.7, 0.8 ppm respectively in the amide. This clearly indicates that the degree and position of stabilisation of the positive charge has changed. Comparison of the chemical shifts of the central carbon atom in these two examples also reflects this change - 162.4 ppm in the carbamate vs. 178.7 ppm in the amide.

Our results may be explained by considering the energy profiles of the two competing reactions.

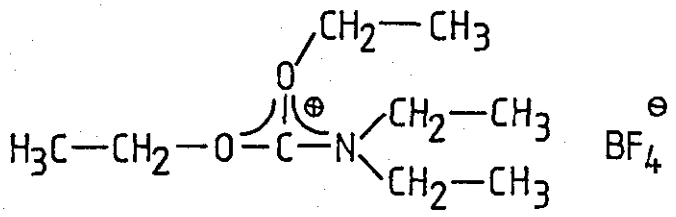


In Alder's reaction at room temperature reaction by Route 2 was found to be reversible, whereas reaction by Route 1 was irreversible i.e. $\Delta G_1 > \Delta G_2$ and $\Delta G_1^{\ddagger} > \Delta G_2^{\ddagger}$.

Thus on lowering the reaction temperature preference is given to *Route 2 where* $\Delta G^{\ddagger}$ *is less than* $\Delta G^{\ddagger}$, *and the kinetic product is formed.*

2.2.9.3 Alkylation of ethyl N,N-diethylcarbamate

Ethylation of the carbamate with triethyloxonium tetrafluoroborate gave the results shown in table 4. A single product was formed, but the reaction did not go to completion.



The O-alkylated product was identified from the ^{13}C nmr data. The methylene carbons attached to the nitrogen atom give a peak at 45.1 ppm, a downfield shift of 3.5 ppm. The corresponding methyl carbons give a peak at 14.5 ppm compared with 13.8 ppm in the carbamate, a *downfield shift of 0.7 ppm. The two ethyl groups on the oxygen atoms* give identical chemical shifts, the methylene carbons being at 74.1 ppm and the methyl carbons at 12.1 ppm. The carbonyl carbon has moved downfield by 5.8 ppm in the alkylated product, giving a peak at 161.8 ppm.

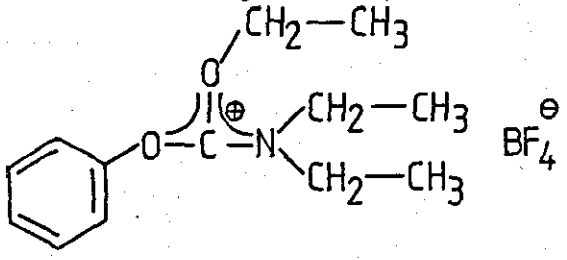
The fact that only two peaks are seen for the two carbons in the ethyl groups reinforces the picture we have for the stabilisation of the positive charge in the molecule, i.e. the charge is stabilised by both oxygen atoms as well as the *nitrogen atom.*

We can once again compare the changes in chemical shifts with those seen in the alkylation of the equivalent N,N-diethylpropionamide (section 2.2.8.5). In the carbamate, the changes in chemical shift *of the methylene and methyl carbons attached to the nitrogen are 3.5 ppm* and 0.7 ppm respectively, compared with 6.1 ppm, 6.2 ppm and 0.7 ppm,

0.8 ppm in the amide. This again illustrates the increased stabilising effect of the three hetero-atoms in the alkylated carbamate compared with only two hetero-atoms in the alkylated amide.

2.2.9.4 Alkylation of phenyl N,N-diethylcarbamate

Treatment of the carbamate with triethyloxonium tetrafluoroborate gave the results shown in table 4. A single product was formed. The reaction did not go to completion.



The product was identified as the O-alkylated product from the ^{13}C nmr data. The methylene carbons next to the nitrogen atom have moved downfield by 3.9 ppm to give a peak at 46.0 ppm. The corresponding methyl carbons have moved downfield by only 0.1 ppm giving a peak at 14.0 ppm. The ethyl group on the oxygen gives two peaks, one at 74.4 ppm and the other at 12.0 ppm, corresponding to the methylene and methyl carbons respectively. The carbonyl carbon has moved from 154.3 ppm in the carbamate to 159.1 ppm in the alkylated product, a downfield shift of 4.8 ppm.

The position of the aromatic carbons has changed very little in the alkylated product. The ortho-carbon has moved upfield by 4.0 ppm whereas the meta-, para- and quaternary carbons have all moved downfield by 2.1 ppm, 2.5 ppm and 0.2 ppm respectively. These small changes are presumably because the aromatic ring is unable to take a major part in the stabilisation of the positive charge. This contrasts with the earlier example of N,N-diethylbenzamide (section 2.2.8.6) where the aromatic ring system could contribute to the stabilisation, and relatively larger changes in chemical shift were noticed for the aromatic carbons.

There was no evidence for the formation of the N-alkylated product.

The ^{13}C nmr of the N-alkylated product is discussed fully in section 2.2.3.1 and is substantially different from that of the O-alkylated product.

2.3 Experimental

These reactions were carried out using as near anhydrous conditions as possible. Where applicable, reagents were either distilled or recrystallised before use. Solvents were purified and dried by conventional methods[85]. The vacuum-line apparatus is fully described in Chapter 3.

^{13}C Nmr spectra were recorded on a Bruker WP80 spectrometer operating at 20.1 MHz, with a pulse width of 2 μsec and a sweep width of 5400 Hz cm^{-1}. The spectrometer was equipped with a variable-temperature probe which enabled low temperature spectra to be run. The broad-band decoupled spectrum was generally obtained initially, followed by the off-resonance spectrum.

'H Nmr spectra were recorded at room temperature on a Perkin Elmer EM360 spectrometer operating at 60 MHz. Low temperature spectra were recorded on a Perkin Elmer R32 spectrometer equipped with a variable-temperature probe operating at 90 MHz.

Infrared spectra were obtained using a Perkin Elmer 177 spectrometer.

Melting points were determined on a Kofler block and are uncorrected.

2.3.1 Reaction of chloroformates with amines

These reactions were carried out under anhydrous conditions according to one of the methods given below. The amines were freshly distilled and stored over 4A molecular sieves. The chloroformates were freshly distilled before use.

Products were identified by comparison of the spectral and physical data of the products with those of authentic samples.

Method 1

This method was used with ether, benzene or toluene as the solvent. The chloroformate (0.025 mole) was dissolved in the solvent (25 cm^3) and cooled to ice-bath temperature under a dry nitrogen atmosphere. The amine (0.025 mole) was added as a solution in the solvent (15 cm^3) over a period of 15 minutes with continuous stirring. The resultant solid was filtered off in a dry-box under nitrogen, and dried overnight in a vacuum dessicator.

Method 2

The amine (0.02 mole) was dissolved in dry dichloromethane (10 cm^3). The chloroformate (0.02 mole) was run in dropwise and with stirring whilst the temperature was held below 5°C using an ice-bath. The mixture was allowed to stand at room temperature for three hours. The solution was then washed with sodium hydroxide solution (2M, 50 cm^3), hydrochloric acid (2M, 50 cm^3) and water (2 x 50 cm^3), then dried over anhydrous magnesium sulphate. Evaporation of the solvent under reduced pressure gave the product.

Method 3

The procedure was as in Method 2 above except that dry benzene (50 cm^3) was used, and the mixture was refluxed for three hours after addition of the chloroformate. Work-up as in Method 2.

Method 4

The procedure was carried out using the vacuum-line. A solution of the amine (3.0 µmole) in the solvent (5 cm^3) was added to a solution of the chloroformate (2.85 m mole in 5 cm^3 of solvent) and stirred at 0-5°C for 30 minutes. The solvent was evaporated off and the flask was evacuated for 2 hours. The product was isolated either as a colourless solid or a clear viscous fluid.

Method 5

The salt was prepared as in Method 4 and then suspended in dry ether (10 cm^3). A solution of the nucleophile (3.0 m mole) in ether (5 cm^3) was then added with stirring at ice-bath temperature. Stirring was continued at room temperature for 15 minutes. The ether

was distilled off together with any excess nucleophile, and an excess of dry ether was added to precipitate the hydrochloride salt. Filtration and evaporation of the dried filtrate yielded the product in 85-93% yield.

2.3.1.1 Reaction of phenyl chloroformate with trimethylamine

The salt was refluxed in dry benzene for 24 hours to give a quantitative yield of trimethylamine hydrochloride and an approximately 50% yield of diphenyl carbonate.

Stirring of a solution of the salt in dry dichloromethane for 12 hours at room temperature gave a similar result.

These results are discussed in more detail in 2.2.1.1.

2.3.1.2 Reaction of phenyl chloroformate with triethylamine

The reaction was carried out as in Method 1 above using benzene as the solvent. A colourless solid was isolated in approximately 66% yield. Attempts to obtain spectra resulted in decomposition. These results are discussed in 2.2.1.2.

Preparation of the salt in dry benzene followed by decomposition in situ according to Method 3 gave phenyl N,N-diethylcarbamate in 97% yield, together with a small amount of diphenyl carbonate.

The same reaction carried out in dichloromethane according to Method 2 gave phenyl N,N-diethylcarbamate in 94% yield, together with a small amount of diphenyl carbonate.

The salt was also prepared in ether according to Method 4 above using a vacuum-line, and yielded a fluffy, colourless solid. Dichloromethane (10 cm^3) was then added and the clear solution was allowed to stir at room temperature for 3 hours. The solvent was evaporated to yield a pale yellow oil. Ether (10 cm^3) was added and the colourless solid was filtered off. The solvent was evaporated from the filtration to give phenyl N,N-diethylcarbamate in 90% yield. Diphenyl carbonate was also formed in very low yield.

The reaction of this salts with various nucleophiles was studied using the general Method 5 above. These were as follows:

(a) With Ethanol - The major products were phenyl N,N-diethylcarbamate and ethyl phenyl carbonate in approximately 5% and 90% yields respectively. Triethylamine hydrochloride was isolated in 84% yield.

(b) With Phenol - The major products were diphenyl carbonate and phenyl N,N-diethylcarbamate in approximately 90% and 5% yields respectively. Triethylamine hydrochloride was isolated in approximately quantitative yield.

(c) With t-Butyl Alcohol - The major product was phenyl N,N-diethylcarbamate (> 90% yield) with a very small amount of diphenyl carbonate. There was no evidence for the formation of t-butyl phenyl carbonate.

(d) With Ethanethiol - The major product was S-ethyl O-phenyl thiocarbonate which was formed in greater than 85% yield. Small amounts of phenyl N,N-diethylcarbamate and diphenyl carbonate could also be detected. Triethylamine hydrochloride was formed in 86% yield.

(e) With Thiophenol - The major product was O-phenyl S-phenyl thiocarbonate which was formed in approximately 80% yield. Small amounts of diphenyl carbonate, phenyl N,N-diethylcarbamate and ethyl phenyl sulphide were also identified as products. Triethylamine hydrochloride was formed in 86% yield.

2.3.1.3 Reaction of phenyl chloroformate with N,N-dimethylbenzylamine

The reaction was carried out as in Method 1 above using ether as the solvent. A colourless, sticky solid was isolated, which readily became a sticky mass on exposure to the atmosphere. No spectra could be recorded. Evaporation of the filtrate yielded phenyl N,N-dimethylcarbamate and benzyl chloride in overall yield of 83% (by weight).

Repeating the reaction in ether on the vacuum-line as in Method 4 gave an opaque, colourless liquid in almost quantitative yield. Analysis by gas chromatography showed this to be a mixture of phenyl N,N-dimethylcarbamate and benzyl chloride.

Preparation according to Method 2 with dichloromethane as the solvent gave phenyl N,N-dimethylcarbamate as the major product together with benzyl chloride. Phenyl chloroformate was also identified in the product mixture.

Reaction of neat phenyl chloroformate with neat N,N-dimethylbenzylamine gave benzyl chloride and phenyl N,N-dimethylcarbamate in quantitative yield after 5 minutes.

Preparation of the salt in toluene according to Method 4 gave an initial bulky, colourless solid. Evaporation of the solvent yielded a colourless, opaque liquid in 82% yield (by weight). This was benzyl chloride and phenyl N,N-dimethylcarbamate.

Preparation according to Method 3 with dry toluene as the solvent gave benzyl chloride and phenyl N,N-dimethylcarbamate as the major products. Phenyl and N,N-dimethylbenzylamine hydrochloride were formed in very low yield.

Using Method 5 with ether as the solvent, the salt was formed and then water (5 cm^3) was added. Phenyl N,N-dimethylcarbamate and benzyl chloride were isolated in 85% yield (by weight).

These reactions are discussed in detail in section 2.2.1.3.

2.3.1.4 Reaction of phenyl chloroformate with N-methylpiperidine

The reaction was carried out using Method 1 with ether as the solvent. The solid that formed in ether decomposed rapidly on isolation to give many unidentifiable products.

When the reaction was carried out in dichloromethane using Method 2, phenyl piperidinylcarbamate was formed in 81% yield (colourless needles from ethanol/water mpt 80-81°C, lit.[26] 83°C).

These results are discussed in detail in section 2.2.1.4.

2.3.1.5 Reaction of phenyl chloroformate with N-methyltetrahydroisoquinoline

The N-methyltetrahydroisoquinoline was prepared from tetrahydroisoquinoline by Eschweiler-Clarke methylation according to the general method of S.H. Pine[86]. Yield = 69%, colourless liquid b.pt. 92.5-93.5°C at 7 mm Hg (lit.[87] 232°C at 763 mm).

The reaction with phenyl chloroformate was carried out as in Method 2 above except that the solution was stirred for 15 hours at room temperature. This yielded a yellow, viscous oil in 73% yield (by weight),

which crystallised slowly on standing. This seemed to be a mixture of diphenyl carbonate and N-(phenoxycarbonyl)tetrahydroisoquinoline. Recrystallisation from methanol: pet. ether (40-60) gave cream crystals of N-(phenoxycarbonyl)tetrahydroisoquinoline in 59% yield overall, m. pt. 95-96.5°C.

IR (C=O) K Br disc 1740 cm^{-1}.

^1H nmr δ ($CDCl_3$) 2.90 (broad t, 2H); 3.78 (broad t, 2H); 4.74 (broad s, 2H); 7.50-8.85 (m, 9H).

The reaction was repeated as above, but the initial products were not washed with sodium hydroxide solution and hydrochloric acid. The solvent was evaporated to yield a yellow oil which contained the expected products, phenyl chloroformate and the hydrochloride salt of the amine.

These results are discussed in more detail in section 2.2.1.5.

2.3.1.6 Reaction of phosgene with 2-(dimethylaminomethyl)phenol

The phenol was prepared by a Mannich-type reaction between equimolar quantities of phenol, dimethylamine and formaldehyde according to the method of H.A. Bruson[88]. Two fractional distillations gave the product in 24% yield, b. pt. 100-102°C at 12 mm Hg (lit.[89] 104°C at 13 mm Hg).

^1H nmr δ ($CDCl_3$) 2.28 (s, 6H); 3.58 (s, 2H); 6.50-7.35 (m, 4H); 9.95 (s, 1H).

Phosgene gas (5.93g, 0.06 mole) was absorbed in dry benzene (60 cm^3) at 0-5°C. To this was added a mixture of the phenol (7.56g, 0.05 mole) and pyridine (3.96g, 0.05 mole) in benzene (5 cm^3) such that the temperature was maintained between 0-5°C. A yellow solid was formed initially, which became red on standing for several hours at this temperature. The solid was filtered off, and the filtrate was washed quickly with ice-cold water (2 x 25 cm^3). The filtrate was then dried over anhydrous magnesium sulphate. Evaporation gave a small amount of brown liquid (1.97g). Spectra were run immediately.

IR (C=O) 1787 cm^{-1}, 1730 cm^{-1}, 1720 cm^{-1} (mixture).

^1H nmr δ ($CDCl_3$) (i) 3.04 (s, 3H); 4.35 (s, 2H); 6.80-7.50 (m, 4H).
(ii) 2.97 (s, 6H); 4.60 (s, 2H); 6.80-7.50 (m, 4H).

These were identified as:

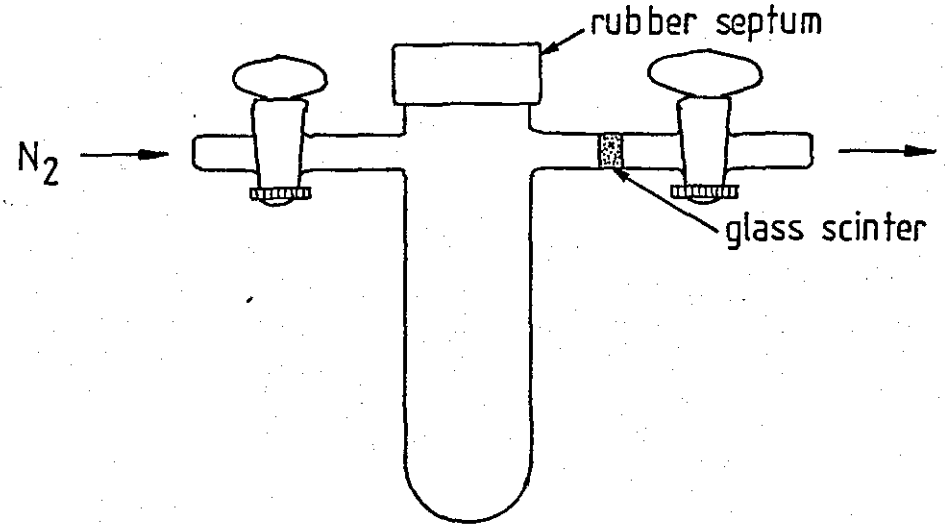
(i) 3-Methyl-2-oxo-dihydro-1,3-benzoxazine

(ii) N,N-Dimethyl-2-(chloromethyl)phenylcarbamate.

These results are discussed in more detail in section 2.2.1.6.

2.3.2 Reaction of chloroformates with amines in the presence of a Lewis acid

These reactions were carried out using a modified method of that given in Klages' paper[14] on the preparation of N-acyl-N,N,N-trialkylammonium hexachloroantimonates. The apparatus used is shown below.



This enabled the simple addition of reagents under a dry nitrogen atmosphere whilst keeping the flask and contents cold. The scinter enabled the product to be easily isolated and washed/recrystallised.

2.3.2.1 Reaction of phenyl chloroformate with triethylamine in the presence of antimony pentachloride

Triethylamine (0.79g, 0.0078 mole) was added to a solution of antimony pentachloride (2.35g, 0.0078 mole) in dry methylene chloride (10 cm^3) at -70°C. Phenyl chloroformate (1.23g, 0.0078 mole) was added to this solution and the reaction was left at -70°C for 2 hours. The solution was allowed to warm to -30°C and then stored under nitrogen at this temperature for 7 days. The pale brown solid was filtered off and washed at -70°C with methylene chloride (2 x 10 cm^3). The solid

was then dried under vacuum at -50°C for 6 hours, and for a further 6 hours at room temperature.

Yield = 1.28g (29% by weight), pale brown solid, m. pt. 76-80°C (dec.).
IR (C=O) no peak visible (Nujol).
^{13}C nmr ppm (SO_2/CD_2Cl_2) 8.7; 47.1. (lit.[50] for $H\overset{+}{N}Et_3Cl^-$ ppm (D_2O, dioxane) 9.5; 47.8).

2.3.3 Reaction of chloroformates with amines in the presence of triethyloxonium tetrafluoroborate

This reaction was carried out using a modified method of that given in Paukstelis' paper[13] on N-acyl-N,N,N-trialkylammonium fluoroborates. Apparatus as shown in section 2.3.2 above.

2.3.3.1 Reaction of phenyl chloroformate with triethylamine in the presence of triethyloxonium tetrafluoroborate

Phenyl chloroformate (1.56g, 0.01 mole) was dissolved in ether (20 cm^3) and cooled to -70°C under a nitrogen atmosphere. Triethylamine (0.55g, 0.005 mole) was added dropwise to give a voluminous, colourless solid. A further amount of ether (20 cm^3) was added. The reaction was then left to stand for 3 hours at -70°C, and 2 hours at -10°C. It was then recooled to -70°C, and the solution of triethyloxonium tetrafluoroborate (0.95g, 0.005 mole) in methylene chloride (20 cm^3) was added rapidly with vigorous stirring. The solution became clear at this stage and on warming to room temperature colourless crystals were formed. The solvent was evaporated under reduced pressure and the residue was dissolved in methylene chloride (10 cm^3). Ether (20 cm^3) was added to give a colourless solid, and the solution was then cooled for 24 hours in a refridgerator. The product was isolated as a pale brown solid 1.06g, yield = 35% (by weight). M. pt. 61-63°C (small amount), < 78°C (all).

IR (C=O) 1822 cm^{-1} (Nujol).
^{13}Cnmr ppm (CD_2Cl_2) 8.5; 8.8 (impurity); 47.6 (impurity); 55.1; 150.4; 120.3; 130.8; 128.8; 151.8. (lit.[50] for $H\overset{+}{N}Et_3Cl^-$ ppm (D_2O, dioxane) 9.5; 47.8).

2.3.4 Reaction of acyl chlorides with amines

No experimental work carried out.

2.3.5 Reaction of acyl chlorides with amines in the presence of a Lewis acid

These reactions were carried out using a modified method of that given in Klages' paper[14] on the preparation of N-acyl-N,N,N-trialkylammonium hexachloroantimonates. Apparatus as shown in section 2.3.2.

2.3.5.1 Reaction of benzoyl chloride with trimethylamine in the presence of antimony pentachloride

Trimethylamine (1.53g, 0.026 mole) was dissolved in chloroform (15 cm^3) and cooled to -70°C. A solution of benzoyl chloride (3.63g, 0.026 mole) in chloroform (15 cm^3) was added quickly and the mixture was left to stand at this temperature for 30 minutes, during which time a colourless precipitate was formed. Antimony pentachloride (7.73g, 0.026 mole) was added and the mixture was swirled to ensure complete reaction. The reaction was left to stand at -30°C for 1 week.

The pale yellow solid was filtered off and washed with methylene chloride (4 x 10 cm^3) at -70°C. The flask was then evacuated at -50°C for 6 hours to remove solvent.

Yield = 9.73g (76% by weight), pale yellow, free-flowing solid, m.pt. > 100°C (lit.[14] 84-86°C softens at about 75°C).
IR (C=O) 1785, 1725 cm^- (lit.[90] for benzoic anhydride: 1783, 1723 cm^{-1}).
^{13}C nmr ppm (SO_2/CD_2Cl_2) 46.4; 129.7; 131.1; 136.1; 163.5.
(lit.[91] for benzoic anhydride ($CDCl_3$, TMS) 128.9; 130.5; 134.5; 162.3. Lit.[92] for trimethylammonium chloride (D_2O, dioxane) 45.8).

2.3.5.2 Reaction of benzoyl chloride with triethylamine in the presence of antimony pentachloride

Benzoyl chloride (1.21g, 8.6 mmole) was dissolved in methylene chloride (5 cm^3) and cooled to -70°C. A solution of triethylamine (0.87g, 8.6 mole) in methylene chloride (5 cm^3) was added such that

the temperature remained at -70°C. Antimony pentachloride (2.57g, 8.6 mmole) was added over a period of about 1 minute, which on shaking, gave a pale brown solid. The reaction was left to stand at -70°C for 4 hours.

The solid was then filtered off and was washed with methylene chloride (2 x 3 cm^3) at -70°C. The solid was dried under vacuum at between -50° and -20°C, and then finally at 10°C for 1 hour.

Yield = 3.47g (75% by weight), pale brown solid, m.pt. 75-76°C, softens above 70°C (lit.[14] m.pt. 76-77°C (sealed capillary).
IR (C=O) 1809 cm^{-1} (s); 1795 cm^{-1} (s); 1780 cm^{-1} (sh); 1695 cm^{-1} (s).
^{13}C nmr ppm (SO_2/CD_2Cl_2) 8.5; 8.8; 47.4; 52.9; 127.6; 129.6; 130.5; 136.2; 172.0.

2.3.5.3 Reaction of acetyl chloride with triethylamine in the presence of antimony pentachloride

The procedure was that used in section 2.3.5.2 above except that acetyl chloride (0.98g, 12.5 m mole) was used in place of benzoyl chloride, together with equimolar amounts of triethylamine and antimony pentachloride.

Yield = 3.60g (60% by weight), pale brown solid, m.pt. 192-194°C.
IR (Nujol, C=O) 1822 cm^{-1} (minor product).
^1H nmr (SO_2/CD_2Cl_2) 1.47 (t); 2.82 (s, (v. small)); 3.25-3.85 (m).
^{13}C nmr ppm (SO_2/CD_2Cl_2) 7.5 (v. small); 8.9; 47.7; 50.8 (v. small).

2.3.6 Reaction of acyl chlorides with amines in the presence of triethyloxonium tetrafluoroborate

The apparatus used was as shown in section 2.3.2 above.

2.3.6.1 Reaction of acetyl chloride with triethylamine in the presence of triethyloxonium tetrafluoroborate

This reaction was carried out by the general method of Paukstelis[13] using acetyl chloride, triethylamine and triethyloxonium tetrafluoroborate. This gave a tacky cream solid in 28% yield (by weight), which decomposed at room temperature to a brown tar. No spectra were obtained as the product was too unstable.

2.3.7 Reaction of acyl fluorides with amines in the presence of boron trifluoride etherate

Reaction according to the procedure in section 2.3.5.2 gave intractable tars that were not investigated further.

2.3.8 Reaction of N,N-dialkylamides with alkylating agents

The N,N-dialkylamides were prepared according to one of the procedures below. The alkylating agents were prepared according to standard procedures.

The alkylation reactions were carried out under anhydrous conditions using one of the three procedures described below.

(a) Preparation of N,N-dialkylamides

Method A

The amine (0.6 mole, 3 equivalents) was dissolved in diethyl ether (200 cm^3, sodium-dried) and cooled in an ice-bath. A solution of the acid chloride (0.2 mole, 1 equivalent) in diethyl ether (100 cm^3, sodium dried) was added to this solution over a period of twenty minutes, with continuous stirring and cooling. The amine hydrochloride was filtered off, and the filtrate was dried over anhydrous magnesium sulphate. Filtration, and evaporation of the solvent under reduced pressure gave the crude product. Purification by distillation gave the pure amide in yields of 55-70%.

Method B

The amine (0.4 mole, 2 equivalents) was dissolved in distilled chloroform (100 cm^3), and cooled in an ice-bath. The acid chloride (0.2 mole, 1 equivalent) was added to this in a dropwise manner and with stirring and cooling. The solution was left to stand for an hour at room temperature. The solution was then washed with water (3 x 100 cm^3) and dried over anhydrous magnesium sulphate. Evaporation of the solvent under reduced pressure gave the crude product. Purification by distillation or recrystallisation gave the pure amide in yields of 49-57%.

N,N-Dimethylacetamide

Prepared by method A in 56% yield, b.p. 165-166°C (lit.[93] 165.5°C).

IR (C=O) 1644 cm^{-1}.

^1H nmr δ ($CDCl_3$) 2.05 (s, 3H); 2.89 (s, 3H); 3.00 (s, 3H).

^{13}C nmr ppm (CD_2Cl_2) 20.4; 34.0; 37.0; 169.5.

N,N-Dimethylpropionamide

Prepared by method A in 55% yield, b.pt. 175-176°C (no lit. value).

IR (C=O) 1645 cm^{-1}.

^1H nmr δ ($CDCl_3$) 1.08 (t, 3H); 2.28 (q, 2H); 2.88 (s, 3H); 2.95 (s, 3H).

^{13}C nmr ppm (CD_2Cl_2) 8.4; 25.7; 34.4; 36.2; 172.9.

N,N-Dimethylbenzamide

Prepared by method B in 57% yield, m.pt. 42-43°C (lit.[94] 41-42°C).

IR (C=O) 1630 cm^{-1}.

^1H nmr ($CDCl_3$) 2.90 (s, 6H); 7.22 (s, 5H).

^{13}C nmr ppm (CD_2Cl_2) 36.8; 40.0; 127.1; 128.3; 129.5; 136.6; 171.3.

N,N-Diethylacetamide

Prepared by method A in 68% yield, b.pt. 185-186°C (lit.[95] 185-186°C).

IR (C=O) 1639 cm^{-1}.

^1H nmr δ ($CDCl_3$) 1.10 (t, 3H); 1.17 (t, 3H); 2.05 (s, 3H); 3.30 (q, 2H); 3.40 (q, 2H).

^{13}C nmr ppm (CD_2Cl_2) 12.1; 13.2; 20.3; 38.9; 41.9; 168.6.

N,N-Diethylpropionamide

Prepared by method B in 49% yield, b.pt. 192-193°C (lit.[96] 191°C).

IR (C=O) 1640 cm^{-1}.

^1H nmr δ ($CDCl_3$) 0.95-1.45 (m, 9H); 2.34 (q, 2H); 3.32 (q, 2H); 3.37 (q, 2H).

^{13}C nmr ppm (CD_2Cl_2) 8.6; 12.1; 13.3; 25.2; 39.1; 40.9; 171.8.

N,N-Diethylbenzamide

Prepared by method A in 70% yield, b.pt. 114-115°C at 2.5 mm (lit.[94] 280-282°C at 760 mm).

IR (C=O) 1631 cm^{-1}.

^1H nmr δ ($CDCl_3$) 1.16 (t, 6H); 3.34 (v. broad q, 4H); 7.31 (s, 5H).

^{13}C nmr ppm (CD_2Cl_2) 13.5; 43.5; 126.4; 128.5; 129.1; 137.5; 171.3.

(b) Preparation of alkylating agents

Preparation of trimethyloxonium tetrafluoroborate

This was prepared according to the method of Meerwein[97]. Yield = 89%, colourless crystals, m.pt. 140-143°C (dec.) (lit.[97] 141-143°C). Stored at -30°C.

^{13}C nmr ppm (SO_2/CD_2Cl_2) 78.8.

Preparation of triethyloxonium tetrafluoroborate

This was prepared according to the method of Meerwein[98]. Yield = 85%, colourless crystals, m.pt. 90-92°C (dec.) (lit.[98] 91-92°C). Stored under ether at -30°C.

^{13}C nmr ppm (CD_2Cl_2) 12.2; 84.4.

(c) General alkylation procedures

Alkylation with trimethyloxonium tetrafluoroborate

Method A - in SO_2/CD_2Cl_2

Trimethyloxonium tetrafluoroborate (0.0012 mole) was placed in a clean, dried nmr tube under a dry nitrogen atmosphere. Dried sulphur dioxide (approx. 0.2 cm^3) was condensed into the tube which was then sealed with a rubber septum. The tube and contents were kept at -50°C whilst d_2-methylene chloride (0.1 cm^3) was injected to provide a lock for the spectrometer, followed by the material to be alkylated (0.001 mole). The tube and contents were allowed to come slowly to -20°C at which temperature the ^{13}C nmr spectrum was run generally after 12 hours. Prolonged storage of samples was carried out at -25°C.

Method B - in CD_2Cl_2

Trimethyloxonium tetrafluoroborate (0.0012 mole) was placed in a clean, dried nmr tube under a dry nitrogen atmosphere and the tube was sealed with a rubber septum. d_2-Methylene chloride (0.3 cm^3) was added to give a suspension of the salt. The material to be alkylated (0.001 mole) was then injected into the tube and the tube and contents were shaken for 5 minutes at room temperature. The ^{13}C nmr spectrum was generally run after 12 hours by which time all the solid had dissolved. Storage for prolonged periods was carried out at room temperature.

Alkylation with triethyloxonium tetrafluoroborate

Method C - in CD_2Cl_2

The reaction conditions used were as stated above for the trimethyloxonium salt reactions in d_2-methylene chloride, except that the triethyloxonium salt was readily soluble in the solvent at room temperature. ^{13}C Nmr spectra were run on the samples after 12 hours at room temperature.

(d) Alkylation of N,N-dialkylamides

The ^{13}C nmr spectral data given below are only those that relate to the alkylated product. Those due to excess starting material or other by-products such as ether, etc., are not shown but are mentioned in the discussion of these reactions.

2.3.8.1 N,N-Dimethylacetamide

Methylated using method B to give a clear, two-phase solution after 18 hours. The reaction went to completion.

^{13}C nmr ppm (CD_2Cl_2) 14.1; 18.0; 38.7; 41.2; 57.8; 60.5; 174.6; 176.9 (spectrum recorded after 24 hours).

2.3.8.2 N,N-Dimethylpropionamide

Methylated using method B to give a clear solution after 18 hours. The reaction went to completion.

^{13}C nmr ppm (CD_2Cl_2) 8.1; 8.4; 20.6; 25.0; 38.9; 40.7; 57.7; 60.3; 178.1; 179.5 (spectrum recorded after 24 hours).

2.3.8.3 N,N-Dimethlybenzamide

Methylated using method B to give an almost clear solution after 12 hours. The reaction went to completion.

^{13}C nmr ppm (CD_2Cl_2) 38.8; 42.4; 59.4; 62.4; 173.7; 174.3.
Aromatic carbons not assigned (spectrum recorded after 24 hours).

2.3.8.4 N,N-Diethylacetamide

Ethylated using method C to give a clear solution after 12 hours. The reaction went to completion.

^{13}C nmr ppm (CD_2Cl_2) 11.5; 12.2; 13.9; 14.6; 45.5; 47.4; 71.0; 175.8 (spectrum recorded after 24 hours).

2.3.8.5 N,N-Diethylpropionamide

Ethylated using method C to give a clear solution after 12 hours. The reaction went to completion.

^{13}C nmr ppm (CD_2Cl_2) 9.4; 11.7; 12.8; 14.1; 21.1; 45.3; 47.0; 70.8; 178.7 (spectrum recorded after 24 hours).

2.3.8.6 N,N-Diethylbenzamide

Ethylated using both method A and method C to give a clear solution after 12 hours.

^{13}C nmr ppm (CD_2Cl_2) 11.7; 12.6; 14.1; 45.2; 48.3; 73.3; 124.8; 127.4; 130.0; 133.2; 174.3. Reaction went to completion. (Spectrum recorded after 24 hours).

^{13}C nmr ppm (SO_2/CD_2Cl_2) 11.7; 12.8; 14.4; 45.2; 48.4; 73.7; 124.5; 127.2; 130.6; 133.6; 174.2. Reaction did not go to completion. (Spectrum recorded after 5 days.)

2.3.9 Reaction of N,N-dialkylcarbamates with alkylating agents

The N,N-dialkylcarbamates were prepared according to one of the procedures given below. The alkylating agents were prepared according to standard procedures (see section 2.3.8).

The alkylations were carried out using one of the general procedures given in section 2.3.8 above.

(a) Preparation of N,N-dialkylcarbamates

Method A

The amine (0.3 mole, 2 equivalents) was dissolved in diethyl ether (200 cm^3, Na dried) and cooled in an ice-bath. The chloroformate ester (0.15 mole, 1 equivalent) was added to this in a dropwise manner and with stirring and cooling. The solution was left to stand at room temperature for several hours. The colourless amine hydrochloride salt was filtered off and the filtrate dried over anhydrous magnesium sulphate. Filtration and evaporation of the solvent under reduced pressure gave the crude carbamate. Distillation gave the pure carbamate in 42-63% yield.

Method B

The amine (0.2 mole, 2 equivalents) was dissolved in distilled chloroform (150 cm^3) and cooled in an ice-bath. The chloroformate ester (0.1 mole, 1 equivalent) was added to this in a dropwise manner and with stirring and cooling. The solution was left to stand at room temperature for several hours. The solution was then washed with water (3 x 150 cm^3) and dried over anhydrous magnesium sulphate. Evaporation of the solvent under reduced pressure gave the crude carbamate. Distillation gave the pure carbamate in 64-67% yield.

Method C

The chloroformate ester (0.2 mole, 1 equivalent) was added dropwise to an aqueous solution of the amine (0.4 mole, 2 equivalents, 20% solution) with stirring and cooling. The solution was left at room temperature overnight. This was extracted with ether (3 x 100 cm^3), dried over anhydrous magnesium sulphate, and the solvent evaporated under reduced pressure to give the crude carbamate. Purification by distillation or recrystallisation gave the pure carbamate in yields of 39-76%.

Methyl N,N-dimethylcarbamate

Prepared by method C in 39% yield, b.p. 130-131°C (lit.[99] 131°C).
IR (C=O) 1710 cm^{-1}.
^1H nmr ($CDCl_3$) 2.87 (s, 6H); 3.63 (s, 3H).
^{13}C nmr ppm (CD_2Cl_2) 36.1; 52.5; 157.3.

Methyl N,N-diethylcarbamate

Prepared by method B in 64% yield, b.p. 155-156°C (lit.[100] 154-155°C).
IR (C=O) 1703 cm^{-1}.
^1H nmr ($CDCl_3$) 1.09 (t, 6H); 3.25 (q, 4H); 3.63 (s, 3H).
^{13}C nmr ppm (CD_2Cl_2) 13.8; 41.6; 52.2; 156.7.

Ethyl N,N-diethylcarbamate

Prepared by method A in 42% yield, b.p. 166-167°C (lit.[96] 167°C).
IR (C=O) 1699 cm^{-1}.
^1H nmr ($CDCl_3$) 1.10 (t, 6H); 1.21 (t, 3H); 3.24 (q, 4H); 4.07 (q, 2H).
^{13}C nmr ppm (CD_2Cl_2) 13.8; 14.7; 41.6; 60.7; 156.0.

Phenyl N,N-diethylcarbamate

Prepared by method B in 67% yield, b.pt. 128-129°C at 4.5 mm Hg.
IR (C=O) 1720 cm^{-1}.
^1H nmr ($CDCl_3$) 1.21 (t, 6H); 3.38 (q, 4H); 7.15 (m, 5H).
^{13}C nmr ppm (CD_2Cl_2) 13.9; 42.1; 121.9; 125.1; 129.2; 151.8; 154.3.

(b) Alkylation of N,N-dialkylcarbamates

The ^{13}C nmr spectral data given below are only those that relate to the alkylated product. Those due to excess starting material or other by-products such as ether, etc., are not shown but are mentioned in the discussion of these reactions.

2.3.9.1 Methyl N,N-dimethylcarbamate

Methylated using method A to give a clear solution after 12 hours. The reaction did not go to completion.

^{13}C nmr ppm (CD_2Cl_2/SO_2 -20°C) 38.7; 62.6; 158.1 (spectrum recorded after 6 days).

2.3.9.2 Methyl N,N-diethylcarbamate

Ethylated using method C to give a clear solution after 24 hours. The reaction did not go to completion.

^{13}C nmr ppm (CD_2Cl_2) 12.0; 14.6; 45.1; 62.4; 74.4; 162.4 (spectrum recorded after 3 days).

2.3.9.3 Ethyl N,N-diethylcarbamate

Ethylated using method C to give a clear light brown solution after 48 hours. The reaction did not go to completion.

^{13}C nmr ppm (CD_2Cl_2) 12.1; 14.5; 45.1; 74.1; 161.8 (spectrum recorded after 5 days).

2.3.9.4 Phenyl N,N-diethylcarbamate

Ethylated using method C to give a clear solution after 12 hours. The reaction did not go to completion.

^{13}C nmr ppm (CD_2Cl_2) 12.0; 14.0; 46.0; 74.4; 117.9; 127.6; 131.3; 152.0; 159.1 (spectrum recorded after 3 days).

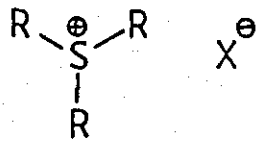
CHAPTER 3

SULPHONIUM SALTS

3.1 Introduction

The usefulness of sulphonium salts as versatile tools in organic synthesis is well-known and several recent reviews are available[3,4,5].

Sulphonium salts (52) are generally more stable than their oxygen analogues. This is emphasised by the fact that trialkyloxonium salts

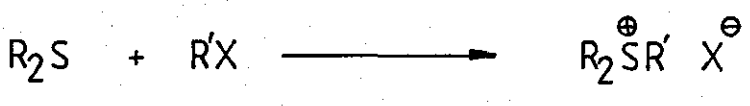


R = alkyl, aryl.
X = hal, etc.

(52)

alkylate dialkyl sulphides to give the corresponding sulphonium salt.

Unlike the oxygen analogues dialkyl sulphides are sufficiently nucleophilic to react with primary alkyl halides under mild conditions to give sulphonium salts (53). These salts are frequently stable,



X = I, Cl, etc..

(53)

easy to handle and crystallise well. Other alkylating agents have been used in these reactions and include alkyl sulphates[102], alkyl sulphonates[103], alkyl fluorosulphates[74], alkyl triflates[104], dialkoxycarbenium tetrafluoroborates[105] and dialkylhalonium salts[106].

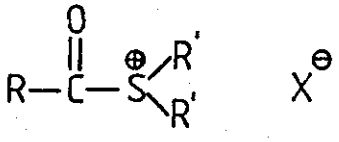
Secondary and tertiary alkyl halides are usually unreactive towards dialkyl sulphides, although activated secondary alkyl halides react in the presence of silver tetrafluoroborate to give quantitative yields of the product[107].

Alkylation of diaryl sulphides by alkyl halides can only be achieved in the presence of silver[108] or mercury(II) salts[109], as the nucleophilicity of the sulphide group is much lower than that of an alkyl sulphide. This reaction appears to involve an S_N2 displacement by sulphide on a silver-complexed halide[110], as silver halide is not

formed until the diphenyl sulphide is added. Alkylation of diphenyl sulphide by trialkyloxonium tetrafluoroborate yields the expected salt in good yield[111].

If the counter-ion is nucleophilic e.g. Cl^-, alkylation of the sulphide is reversible, and the salt can be dealkylated by the halide ion. There is a tendency for the alkyl salt with the lowest molecular weight to be formed in these reactions. Thus, reaction of dimethyl sulphide with allyl iodide in methanolic solution yields trimethylsulphonium iodide[112]. Because of this reaction many sulphonium salts are only isolable when a relatively non-nucleophilic anion is present.

Acyldialkylsulphonium salts (54) have been postulated as inter-

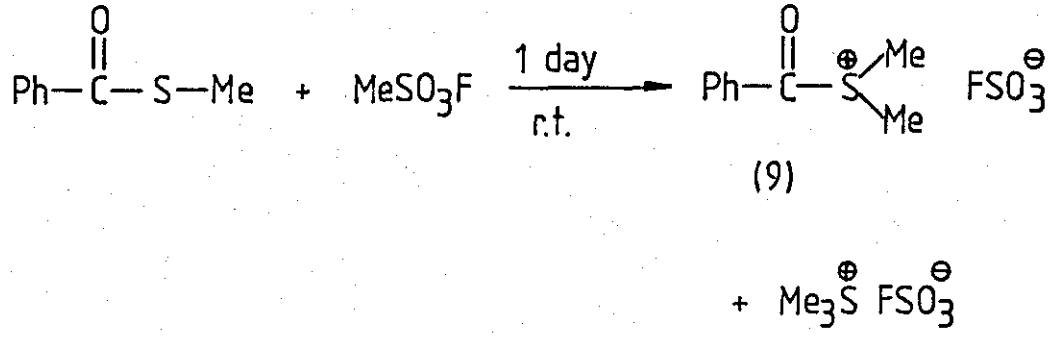


(54)

R=aryl,alkyl.
R'=alkyl.
X=hal.

mediates in the reaction of acyl halides with active sulphides such as episulphides[113] and α-aminosulphides[114]. Acyl halides do not react with simple dialkyl sulphides[115]. Oishi suggested their intermediacy in the reaction of benzoyl chloride with methyl n-octyl sulphide in the presence of silver perchlorate, but did not isolate or characterise them[116]. Minato[18] has reported that the attempted preparation by reaction of benzoyl chloride and dimethyl sulphide in the presence of antimony pentachloride at -70°C proved unsuccessful with only chlorodimethylsulphonium hexachloroantimonate being isolated. Further attempts by Oishi to prepare these salts by the alkylation of S-ethyl thiobenzoate with triethyloxonium tetrafluoroborate or diethoxycarbenium hexachloroantimonate proved unsuccessful although their intermediacy was again suspected[117].

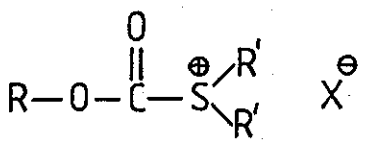
Minato successfully isolated the salt (9) together with the trimethylsulphonium salt in the reaction of S-methyl thiobenzoate with methyl fluorosulphate at room temperature[18].



(9)

The aim of our work was to prepare salts of the type (54) in a pure state, record their 'H nmr and ^{13}C nmr spectra, and to evaluate their synthetic value as acylating agents for weak nucleophiles. We decided to reinvestigate several of the systems described above and our results are described in sections 3.2.4 - 3.2.7 that follow.

Alkoxy/phenoxycarbonylsulphonium salts (11) have not been reported in the literature. These salts could be used for the pro-



(11)

R=alkyl,aryl.

R'=alkyl.

X=hal,etc..

tection of N-, O- and S- groups in synthesis c.f. Chapter 2, N-alkoxycarbonyl-N,N,N-trialkylammonium salts.

We decided to investigate the preparation of these salts (11) using procedures similar to those mentioned above for the acylsulphonium salts. Characterisation using 'H nmr and ^{13}C nmr techniques would give an insight into how the positive charge is stabilised in the molecule. Our results are described in sections 3.2.1 - 3.2.3 and 3.2.8 below.

Salts of type (54) and (11) are extremely hygroscopic. Thus, great care was taken to exclude moisture from the reactions. Much time was spent designing equipment and devising experimental procedures

to achieve these conditions. Section 3.2.9 describes in detail the apparatus and experimental conditions used in these experiments.

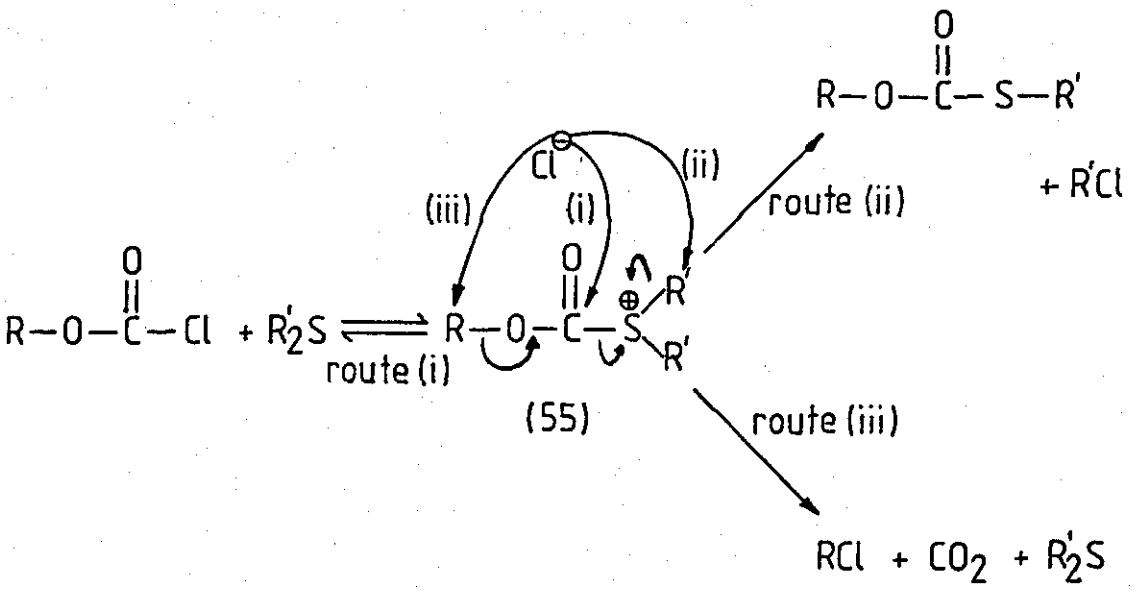
3.2 Preparation and Reactions of α-Carbonyl Sulphonium Salts

3.2.1 Reaction of chloroformates with sulphides

There have been no reported reactions between chloroformates and sulphides. It is unlikely that reaction would occur as acyl chlorides react only with active sulphides such as episulphides[113] and α-amino-sulphides[114] - these latter reactions are discussed further in section 3.2.4.

The reaction below was carried out in order to check this prediction using a simple dialkyl sulphide.

This type of reaction was not investigated in great detail as even if an intermediate of the type (55) is formed, it would readily decompose by any of the three routes shown below in the presence of

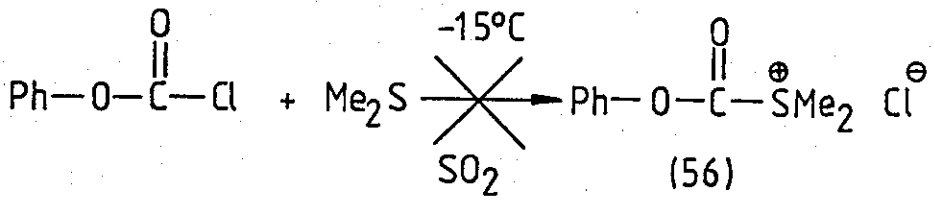


the nucleophilic chloride ion.

3.2.1.1 Reaction of phenyl chloroformate with dimethyl sulphide

After 8 days at -15°C a solution of phenyl chloroformate and dimethyl sulphide in liquid sulphur dioxide shows no sign of reaction.

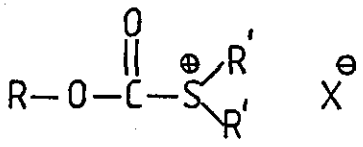
^{13}C Nmr analysis shows only peaks corresponding to the starting



(56)

materials, as expected. There is no evidence for the formation of the intermediate (56).

These results indicate that a more reactive system is needed to achieve alkoxy/aryloxycarbonylsulphonium salts of the type (11) shown below, and that X must be non-nucleophilic.



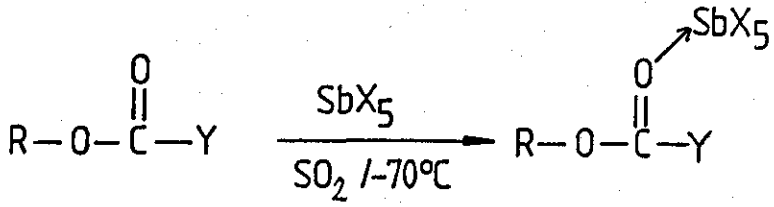
(11)

The following sections (3.2.2 and 3.2.3) describe our attempts to achieve such a system.

3.2.2 Reaction of chloroformates with sulphides in the presence of a Lewis acid

There have been no reported reactions between chloroformates and sulphides in the presence of a Lewis acid.

It is known, however, that chloroformates react with Lewis acids such as antimony pentachloride[45] and antimony pentafluoride[49] to give complexes of the type (57).



(57)

X=F ; Y=Cl.

When R = alkyl, the complex undergoes ionisation to give an alkoxycarbonyl cation, which subsequently fragments to an alkylcarbenium ion and carbon dioxide. Olah[49] has shown that this reaction is

$$(57) \rightleftharpoons [R-\overset{\oplus}{O}=C=O]\ SbX_5Y^{\ominus} \rightleftharpoons R^{\oplus}\ SbX_5Y^{\ominus} + CO_2$$

X=F ; Y=Cl,F.

reversible when R = methyl. When R = aryl, a stable donor-acceptor complex (57) is formed at -70°C which is stable up to -20°C. At higher temperatures bimolecular reactions give diphenylcarbonates. Thus, aryl chloroformates give complexes that act solely as carboxylating agents, and such complexes have been used in Friedel-Crafts acylations.

This latter type of reaction would seem to present us with a possible route to aryloxycarbonylsulphonium salts (58), by reaction of complex (57) with a suitable dialkyl sulphide.

$$(57) \xrightarrow{R'_2S} R-O-\overset{O}{\overset{\|}{C}}-\overset{\oplus}{S}\overset{R'}{\underset{R'}{<}}\ SbX_5Y^{\ominus}$$

(58)

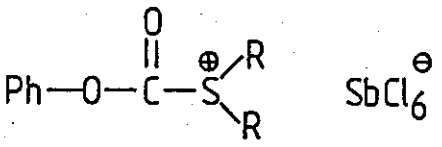
R=aryl.
R'=alkyl.
X=F.
Y=Cl.

We chose to study this reaction using phenyl chloroformate and a range of simple dialkyl sulphides, in the presence of antimony pentachloride.

Antimony pentachloride was chosen as the Lewis acid for several reasons. Firstly, it is easily used as long as precautions are taken to ensure anhydrous conditions, and it readily forms complexes with chloroformates[45]. It also gives hexachloroantimonate ion as the counter-ion which facilitates the isolation of a solid product, is relatively non-nucleophilic and generally maintains its integrity.

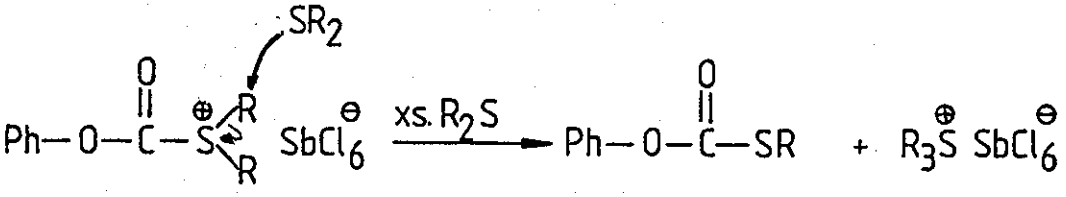
The choice of sulphide is equally important. It is well known that many dialkyl sulphides are sufficiently nucleophilic to react directly with primary alkyl halides under mild conditions to give trialkylsulphonium salts. However, with aryl sulphides alkylation will only take place in the presence of silver[108] or mercury(II)[109] salts. Thus, the simple sulphides dimethyl sulphide, diethyl sulphide and tetrahydrothiophene were used in our investigations.

If the salt (59) is formed in these reactions, then we would



(59)

expect to see the presence of a trialkylsulphonium salt (60) and a thiocarbonic acid ester (61) in the products when an excess of the sulphide is used. This would presumably be formed by the route shown below (equation 6).

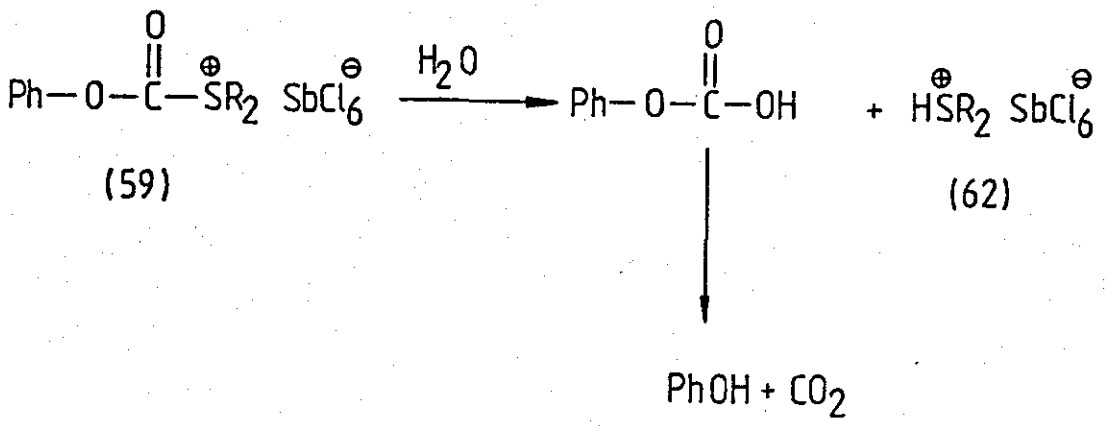


(59) (61) (60)

equation 6.

Indeed, this result would indicate that the salt (59) is formed at some stage as the products ((60) and (61)) cannot be formed by any other route.

Elimination of moisture from these reactions is important as it is to be expected that the salt (59) is extremely susceptible to hydrolysis (equation 7), to give phenol and the protonated sulphonium salt (62)



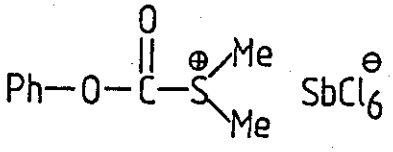
(59) (62)

equation 7

as the products. This reaction is discussed further in the following sections (3.2.2.1, 3.2.2.2 and 3.2.2.3).

3.2.2.1 Reaction of phenyl chloroformate with dimethyl sulphide in the presence of antimony pentachloride

Reaction in methylene chloride at -70°C for 7 days gives a cream-coloured solid, which appears to be hydroscopic. Infrared analysis in acetonitrile gives a carbonyl stretching frequency of 1798 cm^{-1}. This is higher than phenyl chloroformate (1786 cm^{-1}) and S-methyl O-phenyl thiocarbonate (1728 cm^{-1}) and is possibly due to the expected dimethylphenoxycarbonylsulphonium salt (63) which would



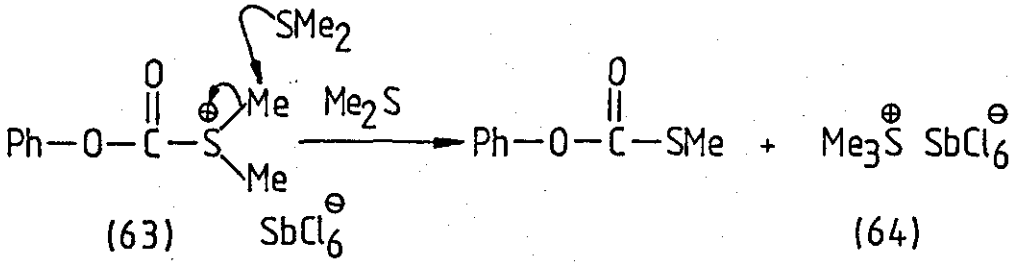
(63)

be expected to have a carbonyl stretch in this area (c.f. N-alkoxycarbonyl-N,N,N-trialkylammonium salts at 1796-1822 cm^{-1}[19]).

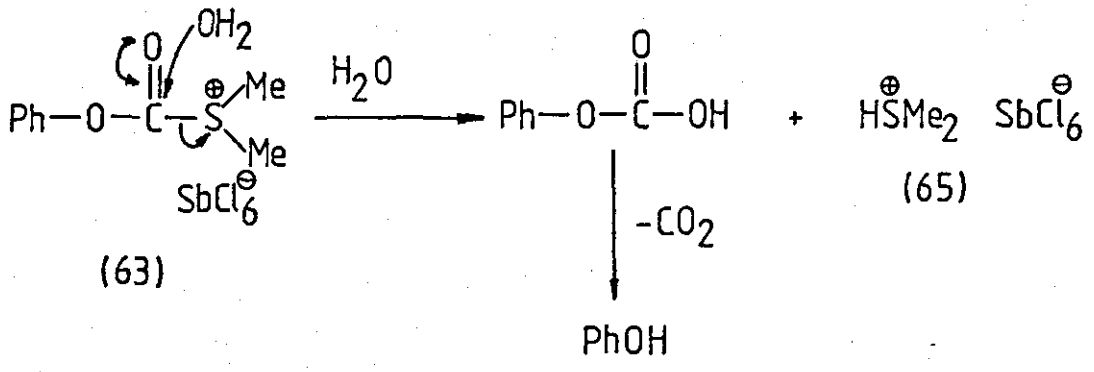
However, analysis using nmr techniques shows this product to be a mixture. Nmr analysis shows the presence of trimethylsulphonium hexachloroantimonate (^{13}C nmr = 27.2 ppm, lit.[118] = 27.5 ppm; no peak in ^{1}H nmr), chlorodimethylsulphonium hexachloroantimonate (^{13}C nmr = 34.9 ppm; ^{1}H nmr = δ 3.19, lit.[18] δ 3.17), dimethylsulphonium hexachloroantimonate (^{13}C nmr = 29.7 ppm; ^{1}H nmr = δ 3.13, no lit. value), S-methyl O-phenyl thiocarbonate (^{13}C nmr = 14.1 ppm, authentic

sample 13.6 ppm[119] for -SMe, aromatics cannot be identified) and a donor-acceptor complex between phenyl chloroformate and antimony pentachloride (^{13}C nmr = cannot be assigned; ^{1}H nmr = δ 7.55-8.45 (m), lit.[49] for PhOCOCl → SbF_5 δ 7.45 (m)).

The presence of trimethylsulphonium hexachloroantimonate can



be explained by the reaction of another molecule of dimethyl sulphide with salt (63) as shown above, which gives the salt (64) and S-methyl O-phenyl thiocarbonate as the products. Hydrolysis of (63) gives the protonated sulphide (65) and phenyl carbonic acid (66), which readily loses carbon dioxide to give phenol. This phenol is not seen



in the products because it is washed out in the work-up procedure. Partial hydrolysis of (63) occurred in the preparation of samples for nmr analysis although the thiocarbonate can be clearly seen in the ^{13}C nmr spectrum.

The formation of chlorodimethylsulphonium hexachloroantimonate (67) is not surprising. It has been reported by Minato[18] that benzoyl chloride and dimethyl sulphide in the presence of antimony penta-

$$Me_2\overset{\oplus}{S}Cl \quad \overset{\ominus}{SbCl_6}$$

(67)

chloride react to give the salt (67). Meerwein[120] also reported that dimethyl sulphide reacts with an excess of antimony pentachloride to give (67) in good yield (unstable on exposure to air and moisture).

$$Me_2S \xrightarrow{\text{xs. } SbCl_5} Me_2\overset{\oplus}{S}Cl \quad \overset{\ominus}{SbCl_6}$$

(67)

Our own experiments suggest that a small amount of trimethylsulphonium hexachloroantimonate is also formed under these conditions.

A similar reaction was carried out using an nmr tube equipped with a rubber septum, with sulphur dioxide as the solvent. The chloroformate was added to a solution of antimony pentachloride at -15°C to give a colourless solution. Addition of one equivalent of dimethyl sulphide gives a clear, yellow solution at -15°C with no solid formation. Nmr analysis shows this to be a mixture of products. The main product is a complex between dimethyl sulphide and antimony pentachloride (68) (^{13}C nmr = 23.5 ppm (broad); ^1H nmr = δ 2.69

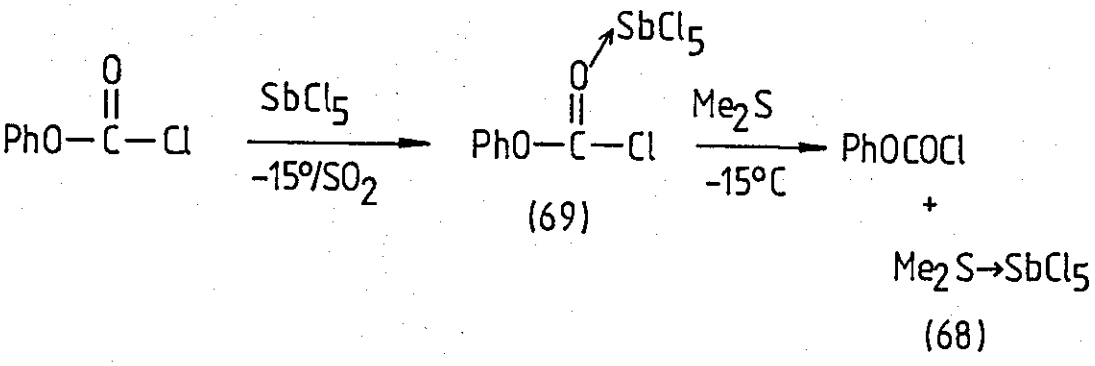
$$Me_2S \longrightarrow SbCl_5$$

(68)

(broad s)). Minor products were the chlorodimethylsulphonium salt (67), the trimethylsulphonium salt (64) and several unidentified products.

Unchanged phenyl chloroformate can be clearly seen in the ^{13}C nmr spectrum, although there is evidence for a small amount of the complexed form being present.

This result is explained by initial formation of the complex (69), which, when dimethyl sulphide is added at -15°C, is attacked to



(69)

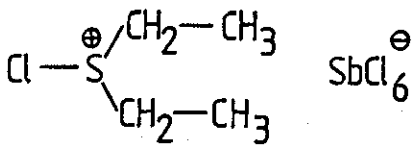
(68)

give free phenyl chloroformate and complex (68). Complexes of this type (68) are well-known and are stable at room temperature in the absence of moisture[121]. Very little chlorodimethylsulphonium salt (67) is formed because there is no excess of free antimony pentachloride available for reaction.

3.2.2.2 Reaction of phenyl chloroformate with diethyl sulphide in the presence of antimony pentachloride

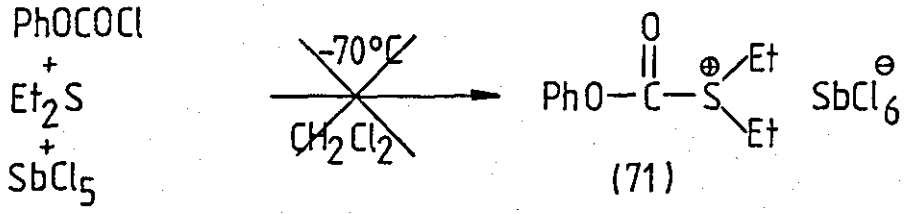
The reaction of equimolar amounts of these materials at -70°C in methylene chloride for 7 days gives a pale yellow solid in low yield.

The ^{13}C nmr spectrum of this product shows only two peaks (42.7 and 7.0 ppm), which are assigned to the chlorodiethylsulphonium salt (70). Salts of this type have been prepared by reaction of the



(70)

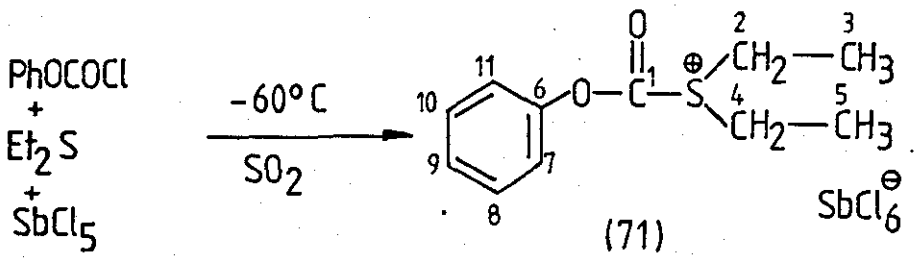
appropriate sulphide with an excess of antimony pentachloride[122]. Thus our result is not unexpected as our reaction conditions would seem to favour the formation of this type of salt. There is no evidence for the formation of a diethylphenoxycarbonylsulphonium salt (71) in this reaction, although the filtrate from the reaction was



not analysed.

The reaction was also studied by carrying out the reaction at -60°C in sulphur dioxide in an nmr tube sealed with a rubber septum. This gives a complicated mixture of products.

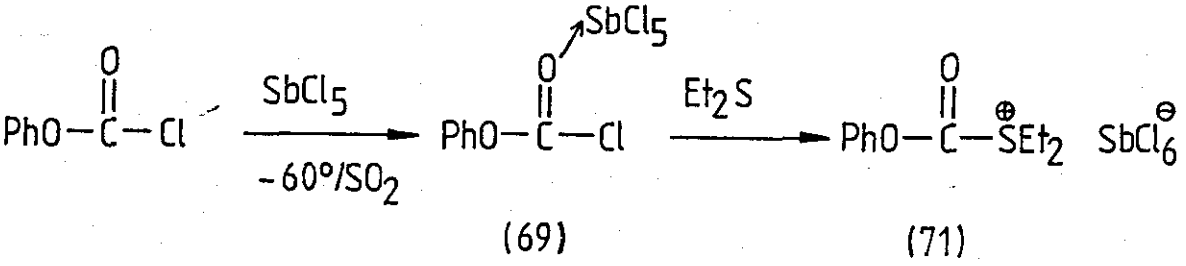
The major product appears to be the expected salt (71). The ^{13}C nmr spectrum shows peaks comparable with those seen in section 3.2.8.1 where S-ethyl O-phenyl thiocarbonate is alkylated on the sulphur atom using triethyloxonium tetrafluoroborate. The ^{1}H nmr spectrum reinforces this view, showing a triplet at δ 1.52 (6H), two quartets at δ 3.38 (4H), and a multiplet at δ 7.17-7.65 (5H). No infrared analysis was carried out.



1.	not assignable	5.	10.7	9.	127.9
2.	36.7 ppm	6.	151.3	10.	130.4
3.	10.7	7.	120.9	11.	120.9
4.	36.7	8.	130.4		

The minor products in the reaction are the chlorodiethylsulphonium salt (70) (^{13}C nmr = 39.4, 9.3 ppm; ^{1}H nmr = δ 3.79, 1.52, lit.[122] for $MeEt\overset{+}{S}ClSbCl_6^-$ δ 3.85, 1.55), triethylsulphonium hexachloroantimonate (^{13}C nmr = 32.4, 8.5 ppm, authentic sample 32.3, 8.4 ppm; ^{1}H nmr = not discernible in spectrum), phenyl chloroformate/antimony pentachloride complex (^{13}C nmr = 161.5 ppm + unassignable aromatic carbons; ^{1}H nmr = δ 7.55 (m), lit.[49] for PhOCOCl → SbF_5 δ 7.45 m), and possibly diethylsulphonium hexachloroantimonate (^{13}C nmr = 35.9, 10.0 ppm; ^{1}H nmr = not discernible in spectrum, no values in the literature). No S-ethyl O-phenyl thiocarbonate is seen in the nmr spectra.

Presumably the salt (71) is formed because diethyl sulphide does not react with antimony pentachloride as easily as does dimethyl sulphide (see section 3.2.2.1), preferentially reacting with the phenyl chloroformate/antimony pentachloride complex (69) at the carbonyl carbon. Hydrolysis of (71) gives phenol, by decarboxylation of phenyl-



(69) (71)

carbonic acid, and the protonated salt. Phenol cannot be identified in the nmr spectra as it is present in very low yield, and the aromatic areas are complicated. An excess of diethyl sulphide in the reaction gives the triethylsulphonium salt and S-ethyl O-phenyl thiocarbonate, albeit in very low yield.

3.2.2.3 Reaction of phenyl chloroformate with tetrahydrothiophene in the presence of antimony pentachloride

Reaction in methylene chloride at -70°C for 7 days gives a bright yellow hygroscopic solid.

The ^{13}C nmr spectrum shows this to be a mixture of products. Peaks for phenyl chloroformate can be identified at 121.3, 128.2, 130.8, 150.4 and 152.4 ppm (lit.[123] 120.5, 127.2, 129.9, 149.3, 151.8 ppm). In the solid it is present as the antimony pentachloride complex, but dissolution in d_3-acetonitrile gives the free chloroformate, the acetonitrile complexing with the Lewis acid. The ^1H nmr also supports this as a multiplet is seen at δ 6.45-7.65 (lit.[49] δ 7.16 (m)), and the IR spectrum shows a peak at 1784 cm^{-1}.

There seems to be a complex mixture of products derived from tetrahydrothiophene. In the ^{13}C nmr spectrum broad peaks are seen downfield from those of "free" tetrahydrothiophene (lit.[124] 31.7, 31.2 ppm) which are attributable to complexes of the sulphide with antimony pentachloride. A similar situation is seen in the ^1H nmr spectrum where two very broad sets of peaks are seen at δ 1.30 - 2.55 and δ 2.55 - 3.95.

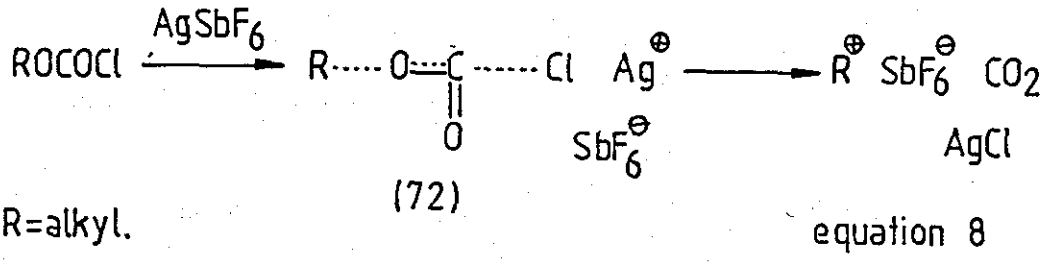
Thus it would seem that the expected phenoxycarbonyltetrahydrothiophenium hexachloroantimonate is not formed under these reaction conditions, presumably because complexes are formed that do not react further.

3.2.3 Reaction of chloroformates with sulphides in the presence of silver hexafluoroantimonate

There are no reports of reactions of this kind in the literature although the equivalent reaction using an acyl chloride in place of the chloroformate is known[116].

The reaction of a chloroformate with the silver salt can formally be considered as proceeding through a carboxylium ion ($ROCO^+$). When alkyl chloroformates are used this can provide a route to high energy carbenium ions which are difficult to prepare by other routes[48,125,126] (equation 8).

Evidence available suggests that the intermediate (72) is best described as a transition state of varying structure in which both carbon-oxygen and carbon-chlorine heterolyses have progressed to varying degrees. An alternative to this involves a slow reaction to a



(72)

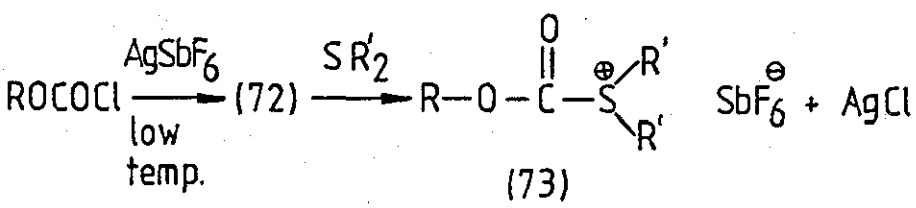
R=alkyl. equation 8

$(ROCO)^+Cl^-Ag^+$ ion triplet with a fast return of chloride occasionally circumvented by loss of carbon dioxide, followed by reaction to products. The overall rate would again be a function of the ease of both carbon-oxygen and carbon-chlorine heterolyses[127].

Aryl chloroformates react with many silver salts to give products with the carbon-oxygen bond intact. Reflux of phenyl chloroformate with silver tetrafluoroborate in chlorobenzene for two hours gives boron trifluoride and phenyl fluoroformate[48]. Similar reactions using silver hexafluoroantimonate produced no evidence for carbon-oxygen cleavage.

Silver hexafluoroantimonate was chosen because the SbF_6^- ion is essentially non-nucleophilic, maintaining its integrity under most conditions.

A range of alkyl and aryl chloroformates were used in our investigations. The choice of dialkyl sulphide was limited to simple sulphides in order to avoid complicated product mixtures (see section 3.2.2).



(73)

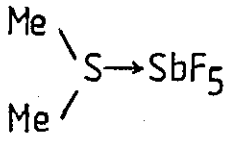
R=alkyl,aryl; R'=alkyl.

An excess of the sulphide would give a trialkylsulphonium salt and a thiocarbonic acid ester by dealkylation of (73), proving the intermediacy of the acyloxysulphonium salt (73).

As in previous reactions in section 3.2.2 every attempt was made to exclude moisture from the reactions.

3.2.3.1 Reaction of phenyl chloroformate with dimethyl sulphide in the presence of silver hexafluoroantimonate

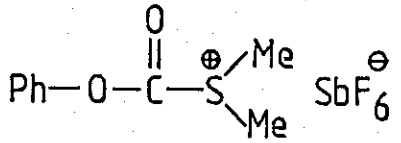
Reaction of equimolar quantities in methylene chloride at -25°C for 22 hours gives a mixture of products. The solid formed initially consists of silver halide and an organic component. The organic component was recrystallised as fine, colourless crystals. ^{13}C Nmr and ^{1}H nmr show peaks at δ 21.1 and 2.50 ppm respectively, which suggest that the product is the complex (74) similar to that seen with antimony pentachloride in section 3.2.2.1 (c.f. $Me_2S \rightarrow SbCl_5$, ^{1}H nmr = δ 2.69 (broad s); ^{13}C nmr = 23.5 ppm (broad). This is



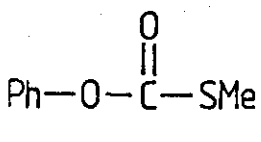
(74)

presumably formed by nucleophilic attack on the hexafluoroantimonate ion by the dimethyl sulphide to give the complex and silver fluoride. This product is also isolated when silver hexafluoroantimonate and dimethyl sulphide are mixed in dichloromethane at room temperature. An orange oil is obtained when the initial filtrate from the reaction is evaporated down. Infrared analysis shows two carbonyl stretching frequencies at 1787 cm^{-1} and 1728 cm^{-1}, and a broad absorption between 3000 cm^{-1} and 3700 cm^{-1}. This indicates the presence of excess phenyl chloroformate (C=O stretch 1786 cm^{-1}), phenol (formed by hydrolysis of either the chloroformate or (75)) and S-methyl O-phenyl thiocarbonate (76) (C=O stretch, authentic sample 1728 cm^{-1}). This is also supported by the ^{1}H nmr data. ^{1}H Nmr gives a singlet at δ 2.38 (-S-Me in thiocarbonate (76), authentic

sample = δ 2.37), a very small singlet at δ 2.57 which is unexplainable, a multiplet at 6.60 - 7.50 (aromatic protons for phenyl chloroformate, phenol and the thiocarbonate (76)), and a singlet at δ 8.60



(75)

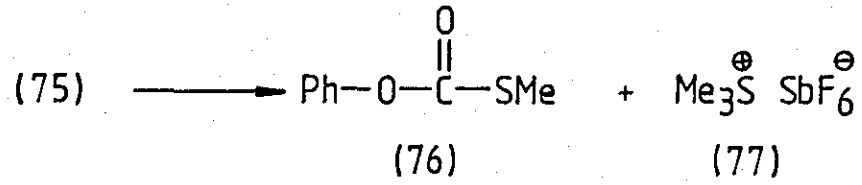


(76)

which is exchangeable with D_2O (-OH in phenol).

Under the same conditions but using two molar equivalents of dimethyl sulphide, similar results are obtained. The fine, colourless crystalline product (74) is isolated in high yield ('H nmr = δ 2.51 (s)). The filtrate yields a colourless, sticky mass which when washed with chloroform and evaporated down gives a clear, yellow oil. Analysis by infrared and nmr techniques shows this to be essentially similar to the mixture of phenyl chloroformate, phenol and thiocarbonate (76) that was obtained with 1 equivalent of sulphide, except that there is no peak in the 'H nmr at δ 2.57. The solid residue from the chloroform washing was not investigated further.

The same reaction using two equivalents of dimethyl sulphide at -25°C for 2 days was studied using a sealed tube in order to exclude moisture during the course of the reaction. The initially isolated solid becomes grey on exposure to light, and 'H nmr analysis in CD_2Cl_2 shows a peak at δ 2.94 (s). This corresponds to the trimethylsulphonium salt (77), which is formed by the nucleophilic attack of dimethyl



(75) (76) (77)

sulphide on the salt (75) (lit.[128] for $Me_3\overset{+}{S}I^-$ = δ 2.88). Evaporation of the filtrate yields a yellow, viscous oil. Infrared and 'H nmr analyses show this to be mostly (> 95%) the expected thiocarbonate (76) with a small amount of phenol (probably formed by hydrolysis of (75)).

There was no evidence for the presence of phenyl chloroformate or the complex (74).

The reaction was also studied using the vacuum-line technique in order to exclude moisture. The silver salt and phenyl chloroformate were initially mixed in methylene chloride at -60°C and left to react for 30 minutes. The sulphide (2 equivalents) was then distilled in, left to stir for 30 minutes, and then the reaction was allowed to warm slowly to room temperature. The reaction was stirred for three days. Initially a dark grey solid is isolated, showing a peak in the ^{1}H nmr spectrum at δ 2.82 (s) which is attributable to the trimethylsulphonium salt (77). Addition of ether to the filtrate gives a colourless solid. ^{1}H Nmr analysis of this product shows a peak at δ 2.50 (s) which corresponds to that for the complex (74). Evaporation of the solvents from the filtrate gives an orange oil, which, when subjected to flask-to-flask distillation on the vacuum-line affords a colourless oil.

Analysis of this oil using infrared, ^{1}H nmr and ^{13}C nmr spectroscopy shows this to be solely the expected thiocarbonate (76).

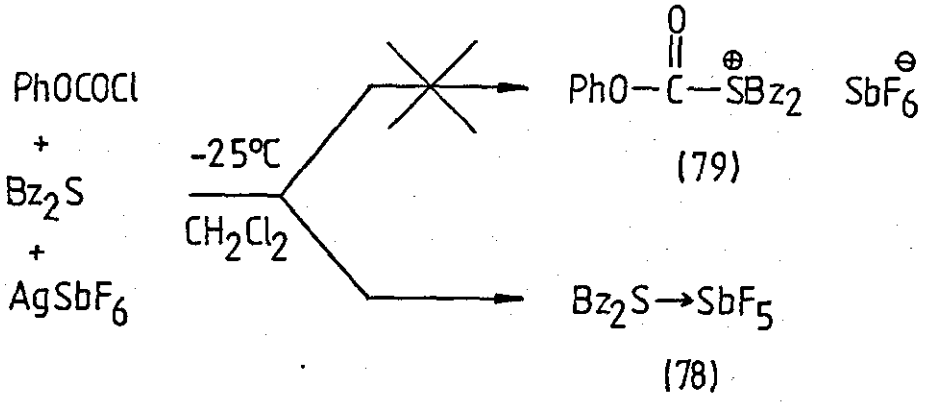
Thus it is clear from these observations that salt (75) is formed in these reactions. It undergoes the expected reactions with excess dimethyl sulphide and water making its isolation impossible under these experimental conditions. The reaction between dimethyl sulphide and silver hexafluoroantimonate is unexpected, but adjustments to experimental techniques seem to almost overcome this problem (compare the results using the vacuum-line (method C) with our earlier results (methods A and B)).

3.2.3.2 Reaction of phenyl chloroformate with dibenzyl sulphide in the presence of silver hexafluoroantimonate

The reaction was studied in methylene chloride at -25°C using two equivalents of dibenzyl sulphide. No solid i.e. silver chloride, was formed initially, which contrasts with our expectations and previous reactions with dimethyl sulphide. Evaporation of the solvent gives an orange, sticky mass. Purification as described in section 3.3.3.2 yields large, colourless needles which darken on ex-

posure to light. 'H Nmr analysis suggests this is the complex (78), with peaks at δ 3.89 (s, 4H) and δ 7.22 (s, 10H), compared with δ 3.54 (s, 4H) and δ 7.18 (s, 10H) for dibenzyl sulphide itself. Treatment of this solid with sodium hydroxide solution (2M) yields the free dibenzyl sulphide. The original filtrate, when the solvent is evaporated, consists almost entirely of phenyl chloroformate with a small amount of phenol formed by hydrolysis. There is no evidence for the formation of the dibenzylphenoxycarbonylsulphonium salt (79) under these reaction conditions.

These results are very similar to those obtained with dimethyl sulphide in that the conditions used favour the formation of this type of complex. Modification of experimental procedures could possibly be used to hinder formation of the complex i.e. the chloroformate should



be allowed to react with the silver salt before the dibenzyl sulphide is added. Unfortunately no further work could be carried out on this reaction.

3.2.3.3 Reaction of methyl chloroformate with dimethyl sulphide in the presence of silver hexafluoroantimonate

Reaction of equimolar quantities of each in methylene chloride at -25°C results in little formation of silver chloride. Treatment of the reaction mixture according to the procedure in section 3.3.3.3 gives fine, colourless needles. 'H Nmr and ^{13}C nmr analyses indicate that the

product is the dimethyl sulphide/antimony pentafluoride complex that we have obtained in several other experiments. The ^{13}C spectrum shows a small peak at 19.8 ppm which is attributable to free dimethyl sulphide (lit.[129] ^{13}C nmr = 19.3 ppm) possibly formed by hydrolysis of the complex by the D_2O used as solvent. Evaporation of the solvent from the initial filtrate gives a small amount of the same complex. Methyl chloroformate is not seen as it is evaporated off with the solvent using the normal work-up procedure.

There is no evidence for the formation of trimethylsulphonium hexafluoroantimonate. It is likely that under these reaction conditions the chloroformate does not react with the silver salt, the silver salt reacting only with the sulphide to give the observed complex.

No further work was carried out on this reaction.

3.2.3.4 Reaction of ethyl chloroformate with dimethyl sulphide in the presence of silver hexafluoroantimonate

The reaction was studied in methylene chloride at -25°C using equimolar quantities of reactants. There is very little silver chloride formed initially. Work-up in the manner described in section 3.3.3.4 gives fine, colourless crystals. Analysis using 'H nmr and ^{13}C nmr techniques shows a single peak in each spectrum, which corresponds to that for the dimethyl sulphide/antimony pentafluoride complex seen in previous experiments. A small quantity of this complex is also recovered from the original filtrate.

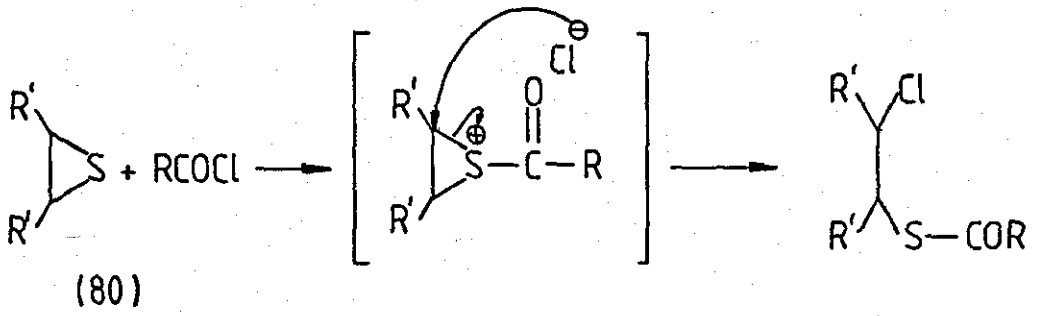
Ethyl chloroformate is not recovered in this reaction because the work-up procedure involves evaporation of volatile materials at reduced pressure.

There is no evidence for the formation of dimethylethylsulphonium hexafluoroantimonate which might have been expected from the fragmentation of ethyl chloroformate in the presence of a silver salt and dimethyl sulphide i.e. the silver salt has reacted preferentially with the sulphide to give the complex and not as expected with the ethyl chloroformate.

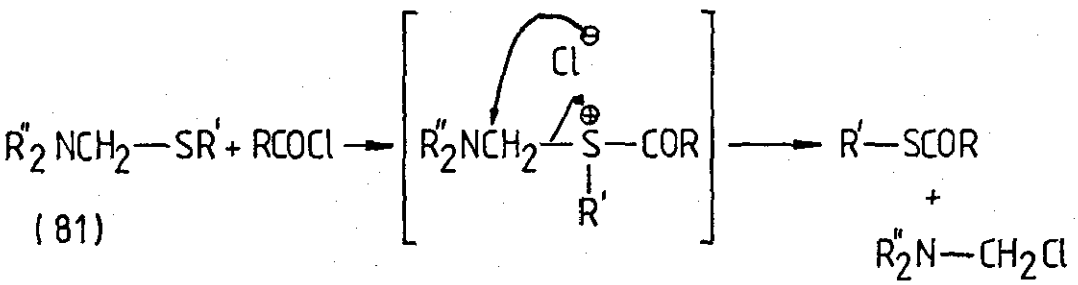
No further work was carried out on this system.

3.2.4 Reaction of acyl halides with sulphides

Reactions of this type are not common. For example, acetyl chloride does not react with dialkyl sulphides even after prolonged periods at 100°C[115]. Indeed, it has been found that only active sulphides such as episulphides[113] (80) and α-aminosulphides[114] (81) react with acyl chlorides.



(80)

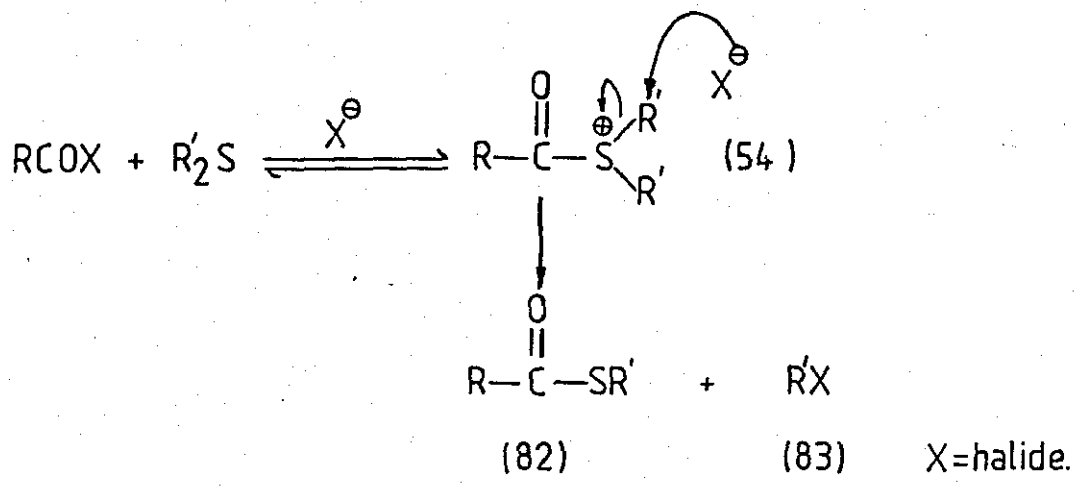


(81)

In both these examples the nucleophilic chloride ion attacks the intermediate acylsulphonium ion, as shown above, to give the corresponding thiocarboxylic acid esters. Thus, it is not possible to isolate these intermediates under these conditions.

The experiment that follows was carried out in order to verify these findings, using an acyl chloride and a simple dialkyl sulphide.

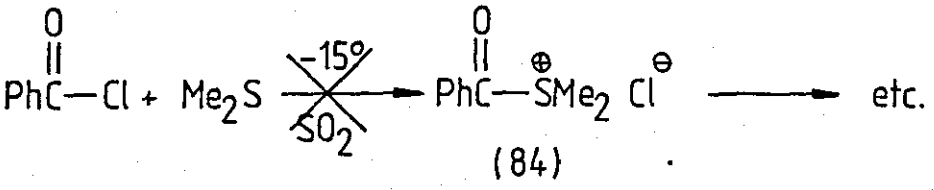
If reaction occurs we would expect to see an alkyl halide (83) and a thiocarboxylic acid ester (82) formed via the intermediate (54) shown.



(82) (83) X=halide.

3.2.4.1 Reaction of benzoyl chloride with dimethyl sulphide

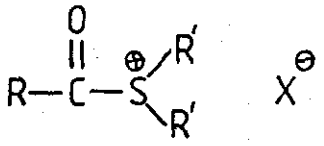
A mixture of the reactants in liquid sulphur dioxide in an nmr tube shows no sign of reaction after 8 days at -15°C. ^{13}C Nmr



(84)

analysis shows only peaks corresponding to the starting materials as expected. There is no evidence for the formation of the intermediate (84).

In order to form acylsulphonium salts of the type (54) shown below it is obvious that a more reactive system is needed, and that X must be non-nucleophilic. The following two sections (3.2.5 and 3.2.6) describe our quest for such a system.

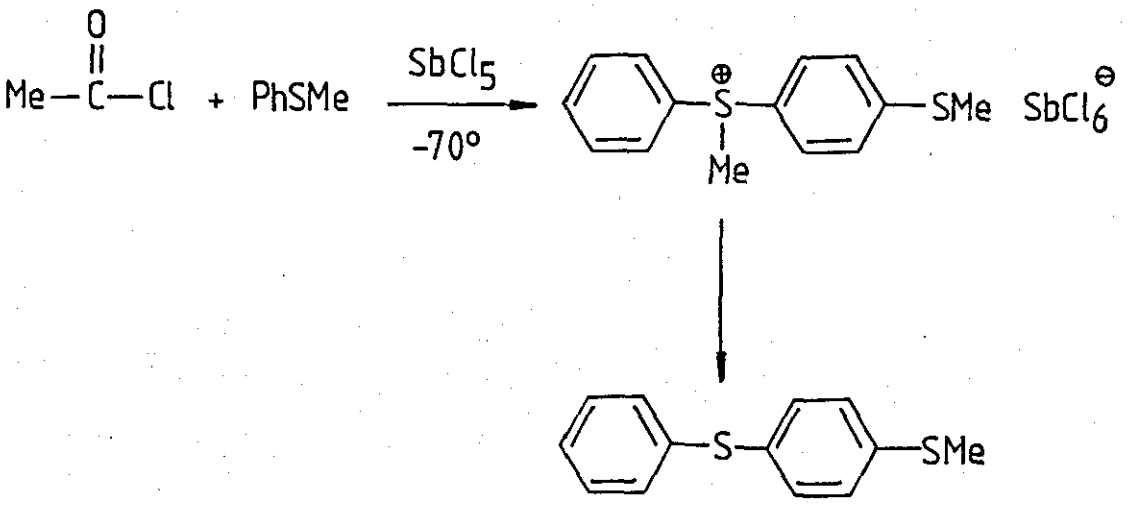


(54)

3.2.5 Reaction of acyl halides with sulphides in the presence of a Lewis acid

There are few reports of reactions of this type[18,116], even though similar reactions involving amines or ethers in place of the dialkyl sulphide are well-known[14,16,130]. In those that have been reported, the acylsulphonium salt was not isolated or characterised.

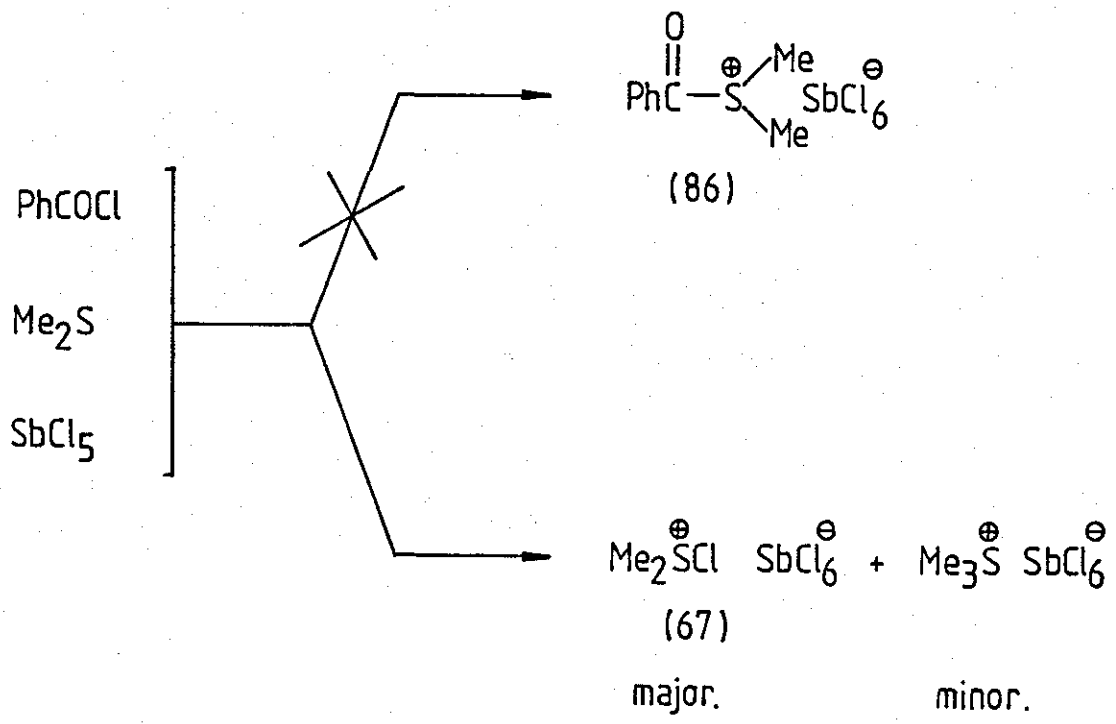
Reaction of acetyl chloride with thioanisole in the presence of antimony pentachloride at -70°C gives the sulphide (85) shown below[116]. Indeed, under the same conditions in the absence of acetyl



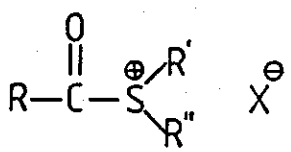
(85)

chloride, the same result was achieved i.e. (85) was formed in almost quantitative yield.

When benzoyl chloride is treated with dimethyl sulphide and antimony pentachloride in methylene chloride at -70°C, chlorodimethylsulphonium ion (67) is formed rather than the benzoyldimethylsulphonium ion (86)[18].



In neither of these latter two reactions was there any evidence for the formation of an acylsulphonium salt (54).



(54)

R=alkyl,aryl ; R'=R''=alkyl,aryl.; X = $SbCl_6$

It was decided to reinvestigate this type of reaction using a selection of acyl halides, dialkyl sulphides and Lewis acids.

The salt (54) could presumably be formed by the reaction of an acylium ion (87) with a dialkyl sulphide at low temperature.

Acyl chlorides react with antimony pentachloride at low temperatures to give either an acylium salt (87) or an acyl chloride/ antimony pentachloride complex (32). Acetyl chloride forms predominantly

$$RC\overset{\oplus}{O}\ X^{\ominus} \xrightarrow[\text{low temp.}]{R'_2S} (54)$$

(87)

$$R-\overset{\displaystyle O\longrightarrow SbCl_5}{\overset{\|}{C}}-Cl \quad (32)$$

the acetylium salt, but benzoyl chloride gives mainly the donor-acceptor complex with only a small amount of the benzoylium salt. Both have been fully characterised by Olah[64] using IR techniques. When antimony pentafluoride is used, both acetyl fluoride and benzoyl fluoride give acylium salts exclusively[64]. These are readily isolable and are reasonably stable in the absence of moisture. It is also known that acyl fluorides complex more readily with antimony pentafluoride than do acyl chlorides with antimony pentachloride[61].

The choice of sulphides was limited to simple dialkyl and diaryl sulphides to facilitate identification of products.

If the acylsulphonium salt (54) is formed, then reaction with an excess of sulphide would yield a trialkysulphonium salt and a thiocarboxylic acid ester (82). This would verify the intermediacy of the

$$(54) \xrightarrow{\text{xs. } R'_2S} R'_3\overset{\oplus}{S}\ X^{\ominus} \qquad R-\overset{\displaystyle O}{\overset{\|}{C}}-SR'$$

(82)

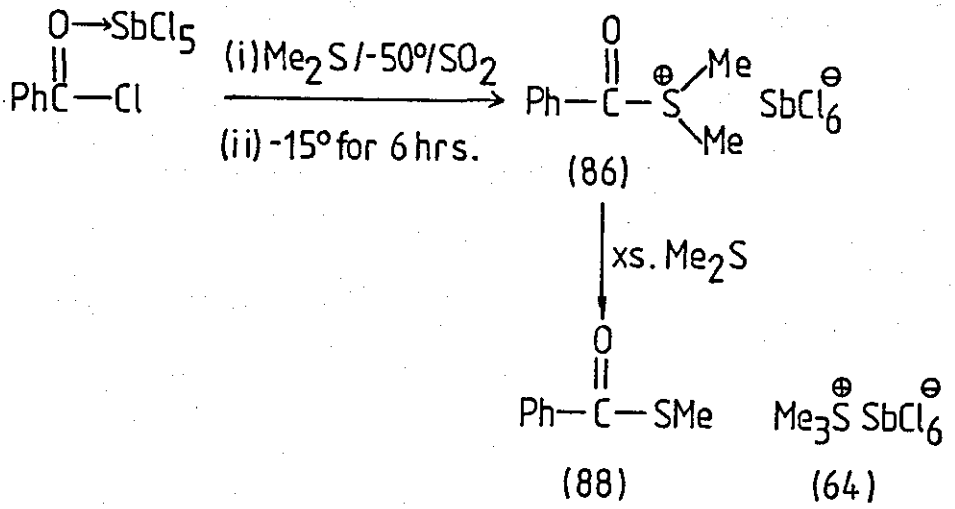
salt (54) as the thiocarboxylic acid cannot be formed by another route.

3.2.5.1 Reaction of benzoyl chloride with dimethyl sulphide in the presence of antimony pentachloride

The reaction was studied using three sets of reaction conditions. The results are discussed below.

When the benzoyl chloride/antimony pentachloride complex is formed first at -50°C in sulphur dioxide, and a ten times excess of dimethyl sulphide is added, an orange solution is obtained after six

hours. Evaporation of the sulphur dioxide gives a sticky, colourless solid which, when washed with ether gives a colourless solid. ^{1}H Nmr analysis shows this to be the trimethylsulphonium salt (64), which must be formed by reaction of the excess dimethyl sulphide on salt (86).

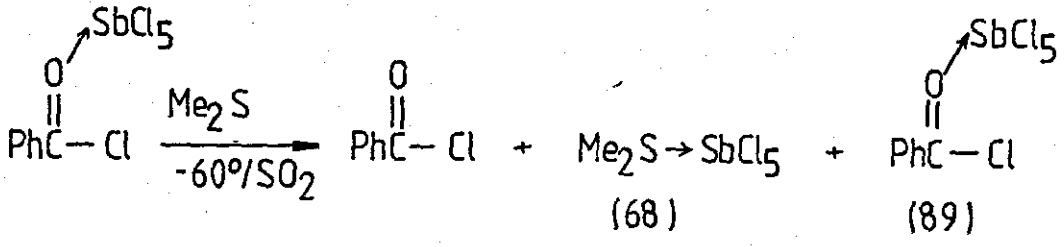


Indeed, analysis of the ether washings shows the presence of S-methyl thiobenzoate (88), (^{1}H nmr = δ 2.42 (s, 3H, -SMe); 7.20-7.75 (m, aromatic); 7.85-8.25 (m, aromatic). Authentic sample = δ 2.39 (s, 3H, -SMe); 7.00-7.50 (m, 3H, aromatic); 7.60-8.00 (m, 2H, aromatic)), and a small amount of benzoic acid presumably formed by hydrolysis of either salt (86) or the benzoyl chloride complex. These results are in direct contrast with the findings of Minato[18] who states that (86) is not formed in this type of reaction.

If dimethyl sulphide (1 equivalent) is allowed to react with antimony pentachloride at -70°C in methylene chloride before the benzoyl chloride is added, then we see very similar results to those reported in section 3.2.2. A cream-coloured solid is isolated, which is a mixture of products. ^{13}C Nmr and ^{1}H nmr analysis using SO_2/CD_2Cl_2 as the solvent system indicate the presence of chlorodimethylsulphonium hexachloroantimonate (major product; ^{1}H nmr = δ 3.07, lit.[18] = δ 3.17; ^{13}C nmr = 35.8 ppm), trimethylsulphonium hexachloroantimonate (minor product; ^{1}H nmr = δ 2.89, lit.[128] = δ 2.88; ^{13}C nmr = 27.4 ppm, lit.[118] = 27.5 ppm) and the benzoyl chloride/antimony pentachloride complex (minor product; ^{1}H nmr = δ 7.35 - 8.25 (m), no lit. value; ^{13}C nmr = complicated aromatic area, carbonyl carbon not seen). Infrared analysis

in d_3-acetonitrile shows a peak at 1775 cm^{-1} which corresponds to free benzoyl chloride. This result is not surprising as a similar effect is seen with phenyl chloroformate antimony pentachloride complexes in acetonitrile (section 3.2.2.1 - 3).

The reaction was also studied at -60°C in sulphur dioxide in an nmr tube using equimolar amounts of reactants. The benzoyl chloride is mixed with the antimony pentachloride at -60°C. After 1 hour the dimethyl sulphide is added, which results in a clear, yellow solution. ^{13}C Nmr analysis shows this to be a mixture of dimethyl sulphide/antimony pentachloride complex (major product; ^{13}C nmr = 22.1 ppm (broad s); no lit. value), benzoyl chloride (major product; ^{13}C nmr = 129.6; 131.8; 132.7; 136.5; 167.6 ppm;, lit. value[131] 128.9; 131.3; 133.1; 135.3; 168.0 ppm), and benzoyl chloride/antimony pentachloride complex (minor product; ^{13}C nmr peaks not assignable). This result is surprising in view of the results we obtained using sulphur dioxide at slightly higher temperatures (-50°C to -15°C in initial experiment above), although a



similar result was seen in section 3.2.2.1 where phenyl chloroformate was used in place of benzoyl chloride.

3.2.5.2 Reaction of benzoyl chloride with diethyl sulphide in the presence of antimony pentachloride

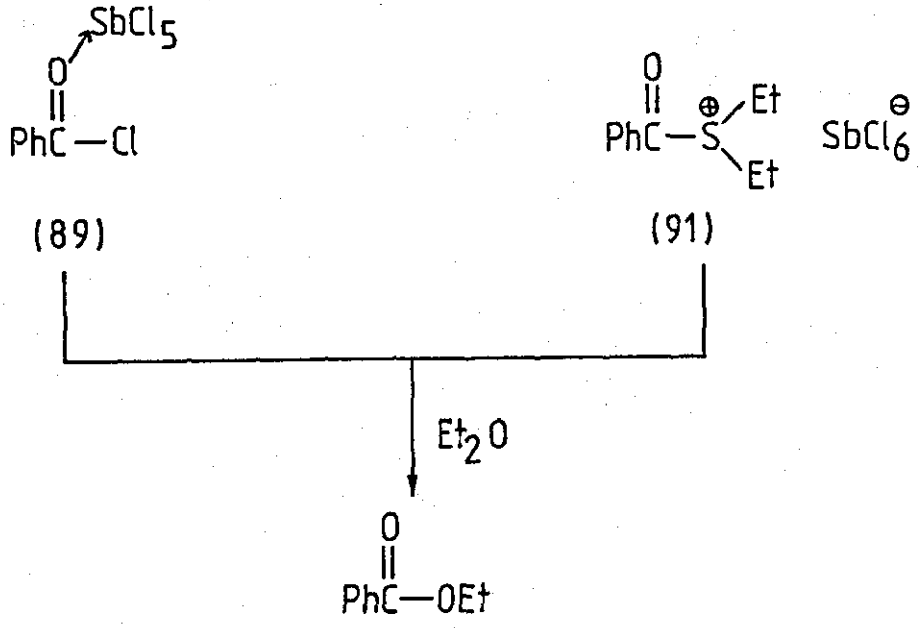
If benzoyl chloride is allowed to react with antimony pentachloride in sulphur dioxide at -60°C a pale yellow solid is formed, which goes quickly into solution when diethyl sulphide (10 x excess) is added at -60°C. After two hours at this temperature the flask is allowed to warm to room temperature in order to evaporate the sulphur dioxide. The dark brown liquid thus formed is washed with ether, the washings being concentrated to give a brown oil. Infrared analysis of

this oil shows carbonyl (stretch) peaks at 1774 cm^{-1} (benzoyl chloride, lit.[132] 1773 cm^{-1}), 1722 cm^{-1} (ethyl benzoate, lit.[133] 1721 cm^{-1}), 1684 cm^{-1}(benzoic acid, lit.[134] 1680-1685 cm^{-1}) and 1663 cm^{-1} (S-ethyl thiobenzoate). The ^1H nmr spectrum shows a triplet at δ 1.28 and a broad quartet at δ 2.55 which are attributable to the diethyl sulphide/antimony pentachloride complex (90). No ^{13}C nmr analysis

$$Et_2S \rightarrow SbCl_5$$

(90)

was carried out on this product. The ^1H nmr also shows aromatic multiplets at δ 7.25 - 7.60 and δ 7.65 - 8.20 which are attributable to a mixture of the products identified in the infrared spectrum. Peaks for the ethyl groups in ethyl benzoate and S-ethyl thiobenzoate are not seen in the ^1H nmr spectrum (very low yields of each when compared with the other products). The ethyl benzoate is presumably formed by reaction of either the benzoyl chloride/antimony pentachloride complex (89) or the benzoyldiethylsulphonium salt (91) with ether at the work-up stage (see Chapter 4 for further examples).



If formed from (91) we would expect to see some triethylsulphonium hexachloroantimonate as well, but our experimental techniques did not allow us to isolate this by-product.

No further work was carried out on this reaction.

3.2.5.3 Reaction of benzoyl chloride with diphenyl sulphide in the presence of antimony pentachloride

No experimental work was carried out on this reaction as it was felt that diphenyl sulphide would not be nucleophilic enough to attack the initially formed benzoyl chloride/Lewis acid complex. This view is reinforced by the fact that aryl sulphides are reported only to be alkylated when either silver[108] or mercury (II)[109] salts are present.

3.2.5.4 Reaction of benzoyl chloride with tetrahydrothiophene in the presence of antimony pentachloride

Reaction of equimolar amounts of these materials in methylene chloride at -70°C for 1 hour, followed by 5 hours at room temperature, gives a tacky, yellow solid. This solid partially liquefies at room temperature.

Attempts to dissolve the solid in various solvents such as $CDCl_3$, CD_2Cl_2, SO_2CD_3CN and D_2O proved fruitless. This suggests that this product is a polymeric material derived from tetrahydrothiophene.

The reaction was not investigated further.

3.2.5.5 Reaction of acetyl chloride with dimethyl sulphide in the presence of antimony pentachloride

Reaction of equimolar amounts of these materials in methylene chloride at -70°C for 1 hour, followed by 5 hours at room temperature gives a pale yellow solid.

^1H Nmr and ^{13}C nmr analysis show this to be mainly the chlorodimethylsulphonium salt (^1H nmr = δ 3.23, lit.[18] = δ 3.17; ^{13}C nmr = 35.7 ppm, no lit. value) with a small amount of trimethylsulphonium hexachloroantimonate (^1H nmr = δ 2.85, lit.[128] = δ 2.88; ^{13}C nmr = 27.2 ppm, lit.[118] = 27.5 ppm) also present. The broad singlet at

δ 3.48 in the 'H nmr spectrum is unexplainable as no corresponding peak is seen in the ^{13}C nmr spectrum.

These results are not surprising as the reaction conditions used allow the sulphide and Lewis acid to come in contact with each other before the acetyl chloride is added.

No further work was carried out on this reaction.

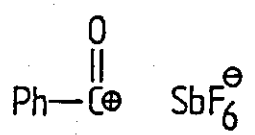
3.2.5.6 Reaction of acetyl chloride with diethyl sulphide in the presence of antimony pentachloride

Reaction of equimolar quantities in methylene chloride at -70°C according to method B in section 3.3.5 gives no solid product. Attempts to crystallise a product from the solution using chloroform were unsuccessful. The reaction was not investigated further.

3.2.5.7 Reaction of benzoyl fluoride with dimethyl sulphide in the presence of antimony pentafluoride

Benzoyl fluoride was allowed to react with an equimolar amount of antimony pentafluoride in sulphuryl chloride fluoride at -60°C in an nmr tube attached to the vacuum line. A colourless solid is formed which goes into solution at -50°C. The sulphide (1 equivalent) is then distilled to give a clear, colourless solution at -50°C.

The 'H nmr spectrum shows that several products have been formed. The singlet at δ 2.45 is attributable to the $Me_2S \rightarrow SbF_5$ complex (see experiments with silver hexafluoroantimonate). The peak at δ 2.88 is due to a small amount of trimethylsulphonium hexafluoroantimonate being present. The peaks at δ 3.11 and δ 2.24 are unexplainable, although the one at δ 2.24 may be due to dimethyl sulphide weakly coordinated to the Lewis acid. The aromatic peaks at δ 7.35-7.80 (m) and δ 7.90-8.15 (m) match closely with the known values for the benzoylium ion (92)



(92)

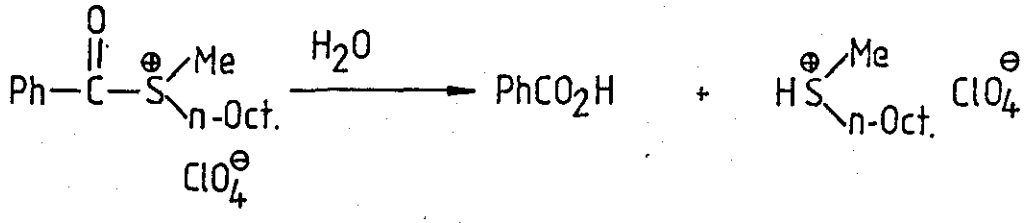
determined by Olah[64].

The ^{13}C nmr spectrum shows only aromatic carbons. No aliphatic carbons can be seen, which may be because a large amount of colourless solid crystallises out in the nmr tube whilst recording the spectrum. Attempts to redissolve this solid proved to be fruitless. The peaks seen in the ^{13}C nmr spectrum compare well with those for the benzoylium ion recorded by Olah[135] (^{13}C nmr = 88.6; 132.7; 141.6; 148.6; 153.9 ppm, lit.[135] = 87.7; 132.9; 141.3; 149.4; 154.8 ppm).

This result would indicate that further work in this area could prove fruitful. Reaction of the benzoylium ion with an excess of dialkyl sulphide should yield the trialkylsulphonium salt and the S-alkyl thiobenzoate. Preparation and isolation of the benzoylium ion (92) would hinder side reactions of the sulphide with free Lewis acid, thus giving a cleaner reaction.

3.2.6 Reaction of acyl halides with sulphides in the presence of silver hexafluoroantimonate

Oishi[116] reported a reaction of this type using silver perchlorate instead of silver hexafluoroantimonate. Oishi found that reaction of benzoyl chloride with methyl n-octyl sulphide in the presence of silver perchlorate at -10°C in methylene chloride gave benzoic acid in 78% yield, presumably formed by hydrolysis of the intermediate salt (93). The salt (93) was not isolated or characterised. He proved the



(93)

presence of an acylsulphonium salt by using an excess of methyl benzyl sulphide in place of methyl n-octyl sulphide which gives methyl thiobenzoate (67.4% yield) and methyldibenzylsulphonium perchlorate (67% yield) as the products.

We decided to reinvestigate this type of reaction using benzoyl

chloride and dimethyl sulphide in the presence of silver hexafluoroantimonate.

Benzoyl chloride reacts with silver hexafluoroantimonate to give the required benzoylium salt (92) in good yield[64].

$$PhCOCl \xrightarrow[-30°/H_3CNO_3]{AgSbF_6} \underset{(92)}{PhC\overset{\oplus}{O}\ \overset{\ominus}{SbF_6}} \quad AgCl\downarrow$$

Reaction of (92) with a dialkyl sulphide would yield the required acylsulphonium salt (94). An excess of dialkyl sulphide would be

$$(92) \xrightarrow[\text{low temp.}]{R'_2S} \underset{(94)}{Ph-\overset{O}{\overset{\|}{C}}-\overset{\oplus}{S}\overset{R'}{\underset{R'}{<}}\ \overset{\ominus}{SbF_6}} \qquad R'=\text{alkyl.}$$

expected to give methyl thiobenzoate and trimethylsulphonium hexafluoroantimonate as the products.

Every effort was made to exclude moisture from the reactions. The techniques are described more fully in sections 3.2.9 and 3.3.6.

3.2.6.1 Reaction of benzoyl chloride with dimethyl sulphide in the presence of silver hexafluoroantimonate

The reaction was studied using several different sets of reaction conditions. The procedures are described in full in section 3.3.6.1.

Reaction of equimolar quantitites of the reactants in methylene chloride at -25°C, followed by 24 hours at room temperature gives an initial colourless solid (presumably silver chloride) after filtration. Evaporation of the solvent from the filtrate gives a colourless cyrstalline mass. ^{1}H Nmr analysis shows this to be a mixture of the dimethyl sulphide/antimony pentafluoride complex (74) (^{1}H nmr = δ 2.47 (s), c.f.

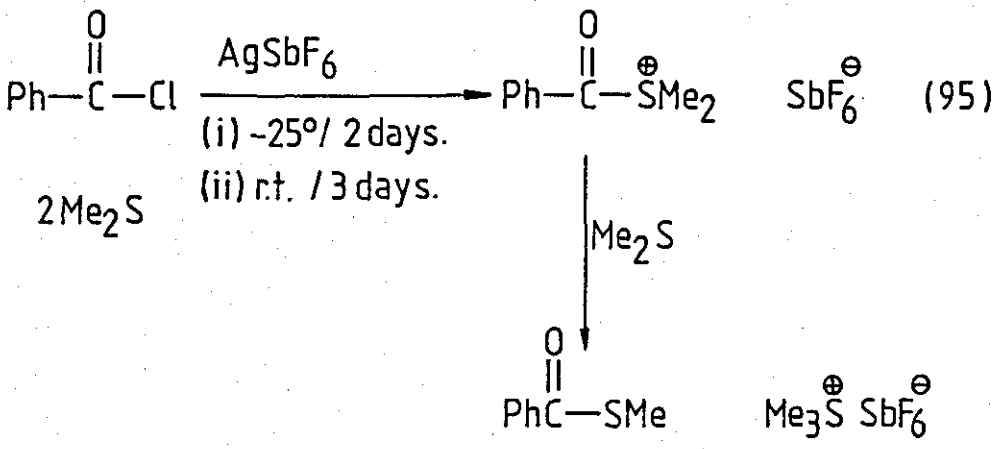
$Me_2S \rightarrow SbF_5$

(74)

section 3.2.3), presumably formed by nucleophilic attack of dimethyl sulphide on the hexafluoroantimonate ion, and benzoic acid. The presence of S-methyl thiobenzoate was not detected.

Using two equivalents of dimethyl sulphide very little silver chloride is formed initially. Addition of ether gives a colourless, crystalline product which turns grey on exposure to light. 'H Nmr and ^{13}C nmr analysis shows this product contains the complex (74). This explains why little silver chloride is formed in this reaction, as the silver salt reacts with the sulphide to give the complex rather than with the benzoyl chloride to give silver chloride and the benzoylium ion. Analysis of the filtrate shows it to be predominantly benzoic acid, probably formed by hydrolysis during the work-up, together with a small amount of the complex (74).

The reaction was also studied using a sealed tube to exclude moisture during the reaction. With two equivalents of dimethyl sulphide and methylene chloride as the solvent, a large amount of insoluble material is formed after 2 days at -25°C and then 3 days at room temperature. Filtration gives a colourless solid that darkens on exposure to light. Evaporation of the solvent from the filtrate yields a pale yellow, sticky solid. 'H Nmr analysis shows this to be a mixture of the complex (74) and S-methyl thiobenzoate ('H nmr = δ 2.38 (s); 7.25-7.65 (m); 7.80-8.20 (m), authentic sample 'H nmr = δ 2.39 (s, 3H, -SMe; 7.00-7.50 (m, 3H, aromatic); 7.60-8.00 (m, 2H, aromatic)). The presence of S-methyl thiobenzoate indicates that the salt (95) has been formed at some stage of the reaction and has then been attacked by a further molecule of the sulphide to give the thiobenzoate and the trimethylsulphonium salt. It is probable that the trimethylsulphonium salt comes out of solution during the reaction, and is filtered off



together with the silver chloride - the initial solid was not analysed in this reaction.

The reaction was investigated further using the vacuum-line apparatus in order to exclude moisture. In order to avoid the side-reaction between the silver salt and dimethyl sulphide, the benzoyl chloride was added to the silver salt first, followed by the sulphide (details in section 3.3.6.1). The reactions were allowed to proceed for 30 minutes at -50°C, and then at room temperature for 3 days.

Using two equivalents of dimethyl sulphide a small amount of solid is formed initially which darkens in light. When ether is added to the filtrate a pale yellow, crystalline solid comes down which is identified as the dimethyl sulphide/antimony pentafluoride complex using nmr techniques (^{1}H nmr = δ 2.47 (s), yield = 34%). The filtrate evaporates down to give a sweet-smelling, yellow solid. No melting point could be obtained. The infrared spectrum shows carbonyl stretch peaks at 1665 cm^{-1} (S-methyl thiobenzoate, authentic sample 1665 cm^{-1}) and 1685 cm^{-1} (benzoic acid, lit.[134] approx. 1680-1685 cm^{-1}). A broad peak at 2400-3600 cm^{-1} also suggests the presence of benzoic acid. ^{1}H Nmr analysis verifies the presence of these products, and also that even under these reaction conditions, a small amount of complex (74) is formed.

Similar results were achieved when a ten molar excess of dimethyl sulphide was used in the reaction. A grey solid is isolated initially. Analysis of this solid using ^{1}H nmr shows it to contain trimethylsulphonium hexafluoroantimonate (^{1}H nmr = δ 2.85 (s), lit.[118] = δ 2.88 for I^-). A tacky, yellow solid is isolated from the filtrate. The infrared spectrum shows carbonyl stretch frequencies at 1667 cm^{-1} (S-methyl thiobenzoate, major product) and 1685 cm^{-1} (benzoic acid, minor product) and a broad peak at 2400-3600 cm^{-1} (O-H stretch in benzoic acid). ^{1}H Nmr analysis also shows the major product to be the thiobenzoate, with a small amount of benzoic acid. There is no evidence for the formation of complex (74).

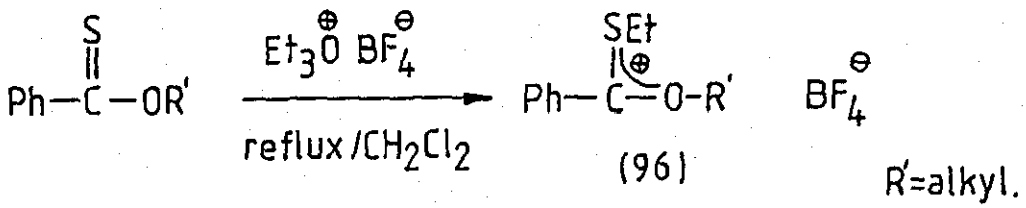
Thus the salt (95) is formed in these reactions, and is dealkylated by the excess dimethyl sulphide to give S-methyl thiobenzoate and the trimethylsulphonium salt. The salt (95) is not isolable under these conditions, and appears to be highly susceptible to hydrolysis by atmospheric moisture.

Further work is needed to determine optimum reaction conditions.

3.2.7 Reaction of thiocarboxylic acid esters with alkylating agents

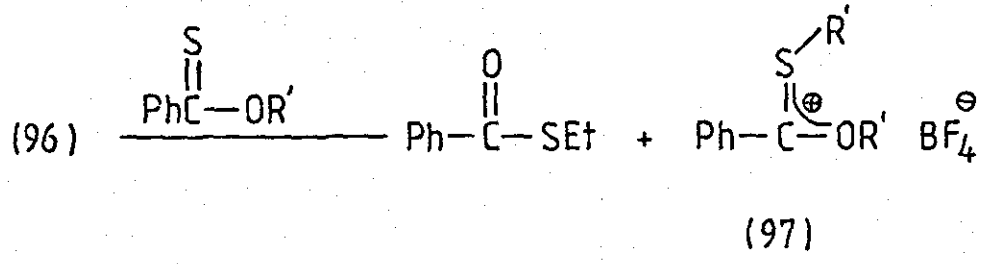
There are several reports of reactions of this type in the literature.

Oishi[136] reported the conversion of O-alkyl thiobenzoates to S-alkyl thiobenzoates in the presence of triethyloxonium tetrafluoroborate. Alkylation occurs on the electron-rich thiocarbonyl sulphur giving the species (96). This is expected to have a high reactivity

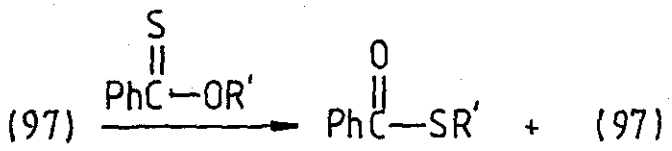


toward nucleophiles because it is structurally related to the diethoxycarbenium ion which is known to be an effective alkylating agent[105].

This species (96) then attacks the remaining O-alkyl thiobenzoate to give S-ethyl thiobenzoate and the alkoxyalkylthiocarbenium ion (97). This ion can then alkylate a further molecule of O-alkyl thiobenzoate

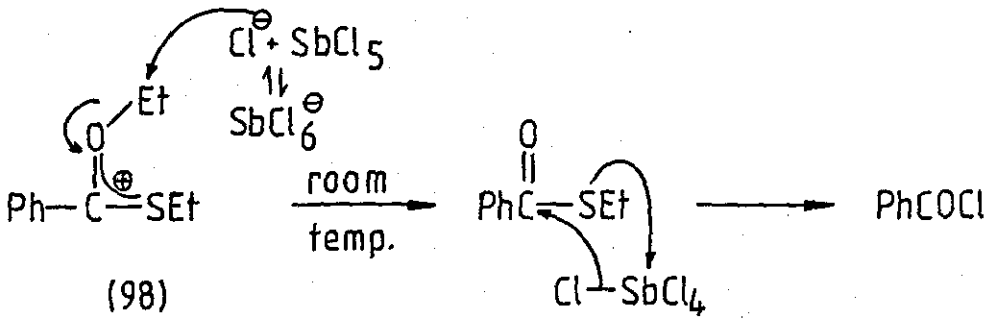


to give S-alkyl thiobenzoate and a further molecule of species (97). This continues until all of the O-alkyl thiobenzoate is consumed.

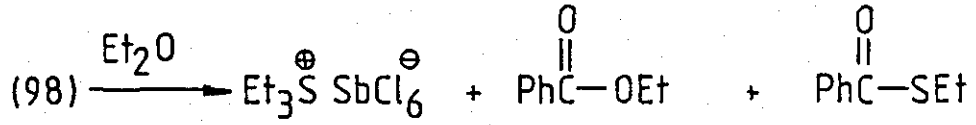


Only a catalytic quantity of the triethyloxonium salt is needed to initiate the reaction.

Oishi has also studied the reaction of the more effective alkylating agent, diethoxycarbenium hexachloroantimonate, with O-alkyl thiobenzoates at lower temperatures[137]. At room temperature, the major product is benzoyl chloride, formed by attack of the hexachloroantimonate ion on the intermediate (98), followed by reaction with the liberated antimony pentachloride. The salt (98) was not char-

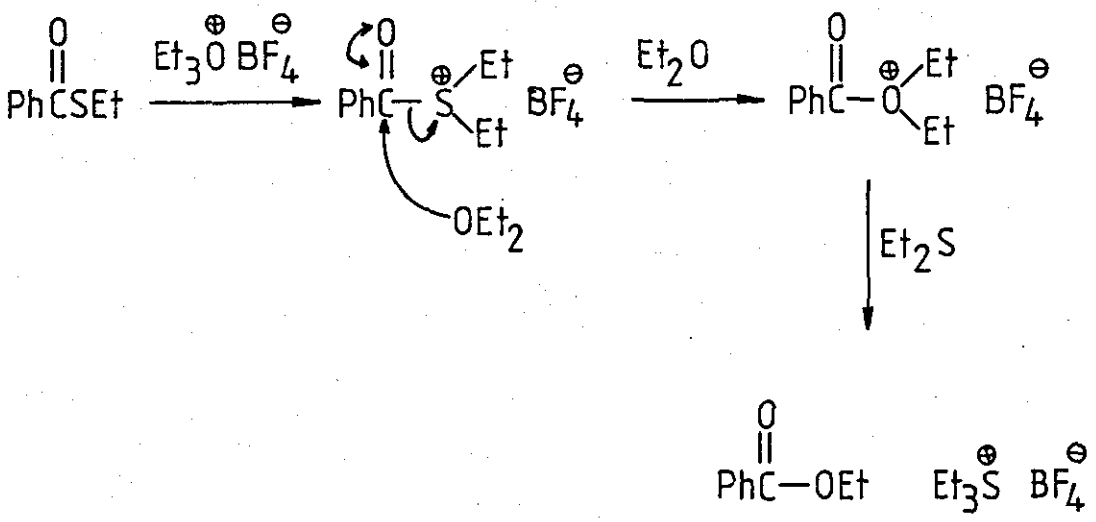


acterised. When the salt (98) is formed at 0°C and then reacted with an excess of ether at reflux the products were identified as triethylsulphonium hexachloroantimonate (24.5% yield), ethyl benzoate and S-ethyl thiobenzoate (relative ratio 2.7:1). When diethyl sulphide

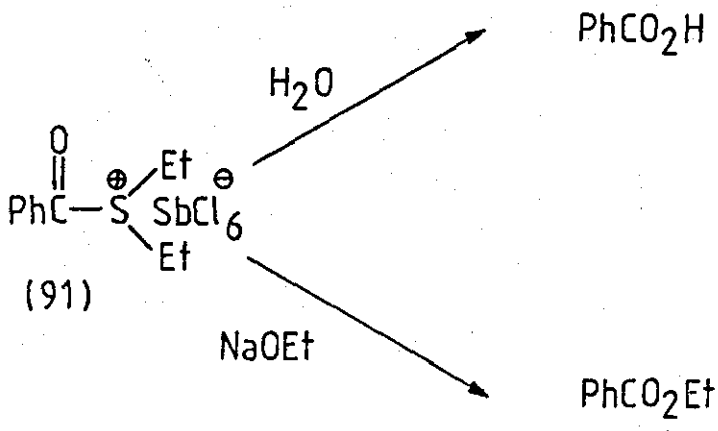


is used in place of ether, the products are S-ethyl thiobenzoate (major), triethylsulphonium hexachloroantimonate and ethyl benzoate (formed by hydrolysis of (98)).

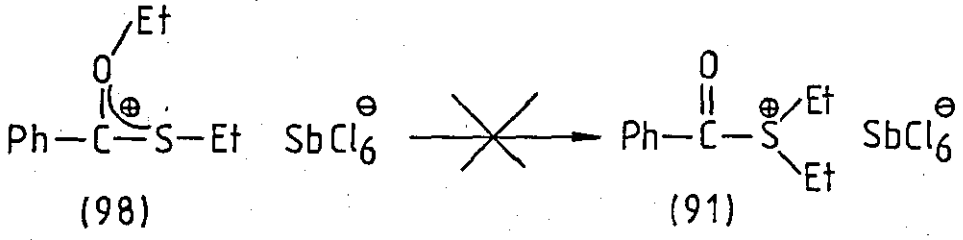
Oishi investigated the reaction of triethyloxonium tetrafluoroborate with S-ethyl thiobenzoate at 85-100°C, and diethoxycarbenium hexachloroantimonate with both S-methyl and S-ethyl thiobenzoate at 0°C and suggested the acylsulphonium salt as an intermediate[117]. Using the triethyloxonium salt the following pathway was proposed:



With diethoxycarbenium hexachloroantimonate at 0°C the salt (91) is obtained as an oily material which reacts with water and sodium ethoxide to give benzoic acid and ethyl benzoate respectively. In neither of these two examples was the acylsulphonium salt characterised. Evidence was presented to support the suggestion that the O-alkylated

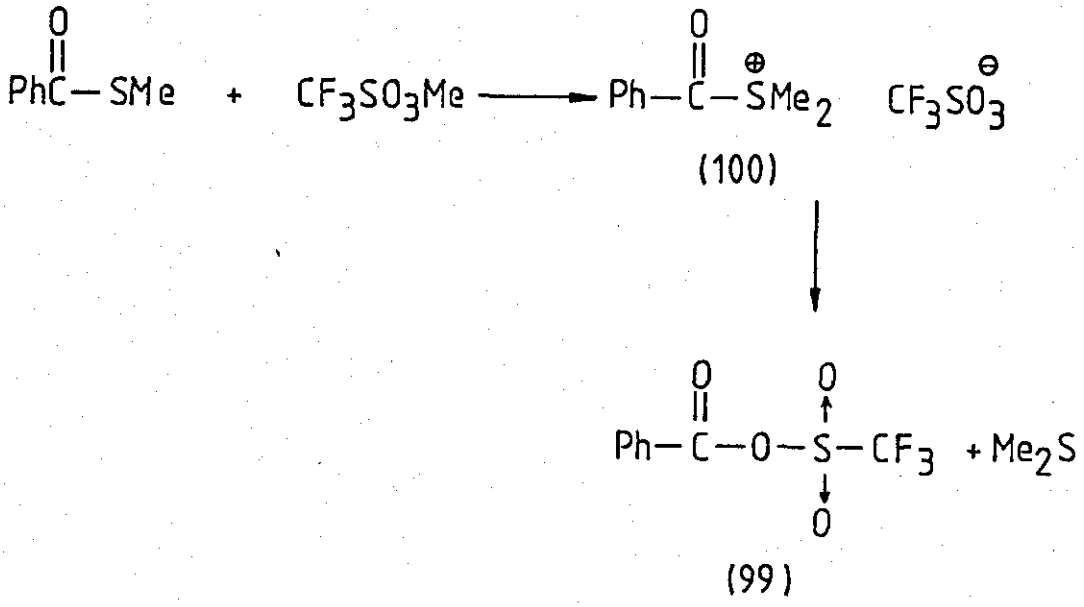


product (98) does not rearrange thermally to the S-alkylated product (91).



Meerwein alkylated thio-γ-butyrolactone with triethyloxonium tetrafluoroborate at room temperature to give only the O-alkylated product[138]. Oishi reinvestigated the reaction and found a mixture of O- and S-alkylated products. Presumably the O-alkylated product is stabilised by some factor, as a similar result is achieved when S-(2-phenylethyl)-thioacetate is alkylated with triethyloxonium tetrafluoroborate[117].

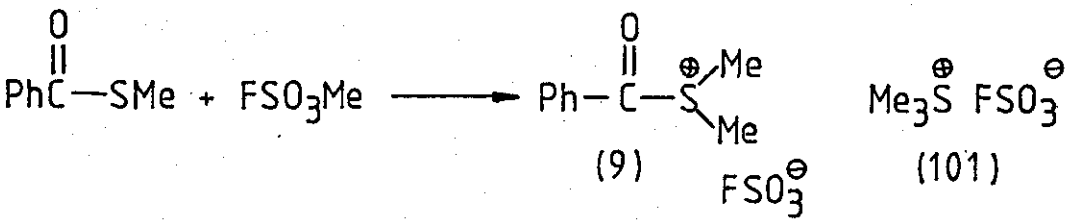
The reactions of S-methyl thiobenzoate with methyl triflate and methyl fluorosulphate have been investigated by Minato[18]. Treatment of the thiobenzoate with methyl triflate in a sealed tube for 3 days at room temperature gives benzoic trifluoromethanesulphonic anhydride (99), presumably formed by nucleophilic attack of the triflate ion on the benzoyldimethylsulphonium ion (100). The anhydride (99) acts as an efficient benzoylating agent. By using methyl fluorosulphate as the alkylating agent, Minato[18] isolated the benzoyldimethylsulphonium salt



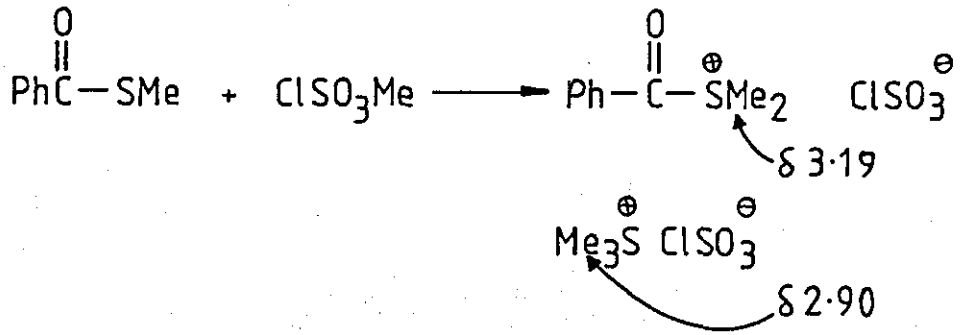
(100)

(99)

(9) as a mixture with trimethylsulphonium fluorosulphate (101) after one day at room temperature in a sealed tube. With methyl chloro-



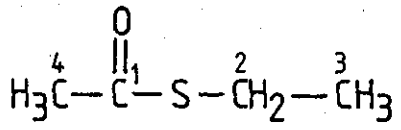
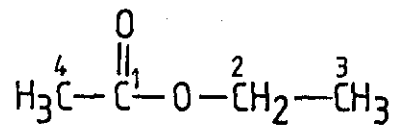
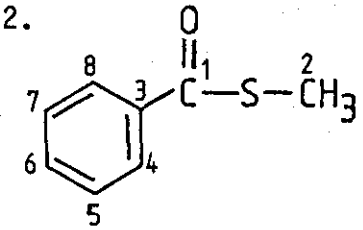
sulphate the corresponding chlorosulphate salts are formed. The ^1H nmr spectra of these chlorosulphate salts have been recorded:



We decided to reinvestigate the alkylation reactions of various S-alkyl thiocarboxylic acids using ^{13}C nmr techniques.

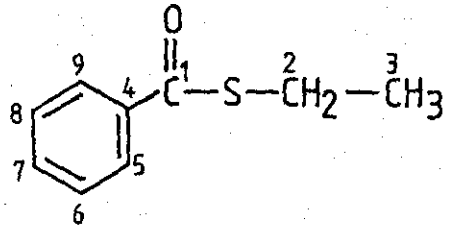
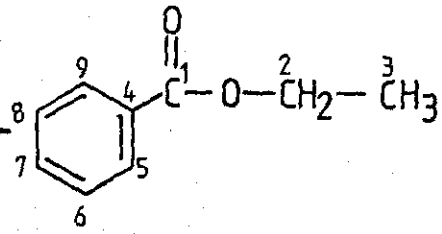
Our reactions were carried out in nmr tubes sealed with a rubber septum which facilitates the addition of the reactants under anhydrous conditions.

Table 5

	Thiol Ester	Conditions[a]	Products	
1.		$Et_3O^{\oplus}\ BF_4^{\ominus}$ / CD_2Cl_2, r.t.		$(H_3C-CH_2)_3S^{\oplus}\ BF_4^{\ominus}$
	1. 195.6 ppm 3. 15.1 2. 23.5 4. 30.9		1. not seen 3. 14.7 2. 61.6 ppm 4. 20.7	1. 32.7 ppm 2. 8.5
				$(H_3C-CH_2)_2O\rightarrow BF_3$ complex
				1. 69.2 ppm 2. 13.6
2.		$Me_3O^{\oplus}\ BF_4^{\ominus}$ / CD_2Cl_2/SO_2, -20°	Small amount	$(H_3C)_3S^{\oplus}\ BF_4^{\ominus}$
	1. 192.0 ppm 5. 128.5 2. 11.6 6. 133.2 3. 137.1 7. 128.5 4. 127.1 8. 127.1		1. 26.2 ppm	

(a) See experimental section for full details.

Table 5 cont.

	Thiol Ester	Conditions[a]	Products	
3.		$Et_3\overset{\oplus}{O}\ \overset{\ominus}{BF_4}$ CD_2Cl_2, r.t.		$(H_3\overset{2}{C}-\overset{1}{C}H_2)_3\overset{\oplus}{S}\ \overset{\ominus}{BF_4}$ 1. 33.0 ppm 2. 8.6 $(H_3\overset{2}{C}-\overset{1}{C}H_2)_2O\rightarrow BF_3$ complex 1. 70.0 ppm 2. 13.4

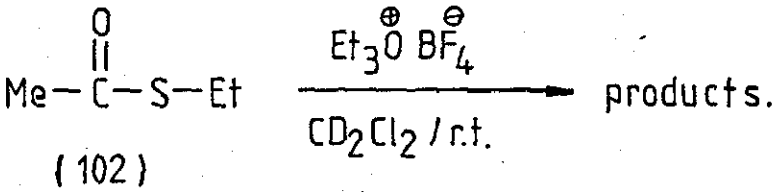
1. 192.0 ppm
2. 23.3
3. 14.6
4. 137.3
5. 127.1
6. 128.5
7. 133.1
8. 128.5
9. 127.1

1. ~ 165.1 ppm
2. 61.1
3. 14.6
4. not assigned
5.
6.
7. not assigned
8.
9.

(a) See experimental section for full details.

3.2.7.1 Alkylation of S-ethyl thioacetate

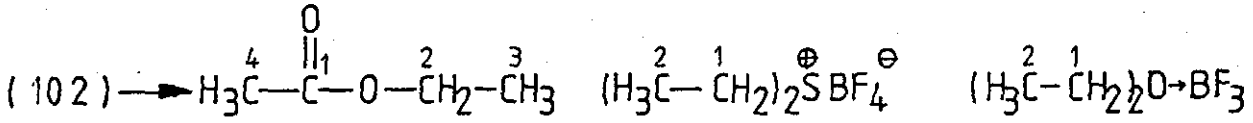
Ethylation using triethyloxonium tetrafluoroborate gave the results shown in table 5. ^{13}C Nmr shows the presence of several products, and the reaction does not go to completion under these conditions.



(102)

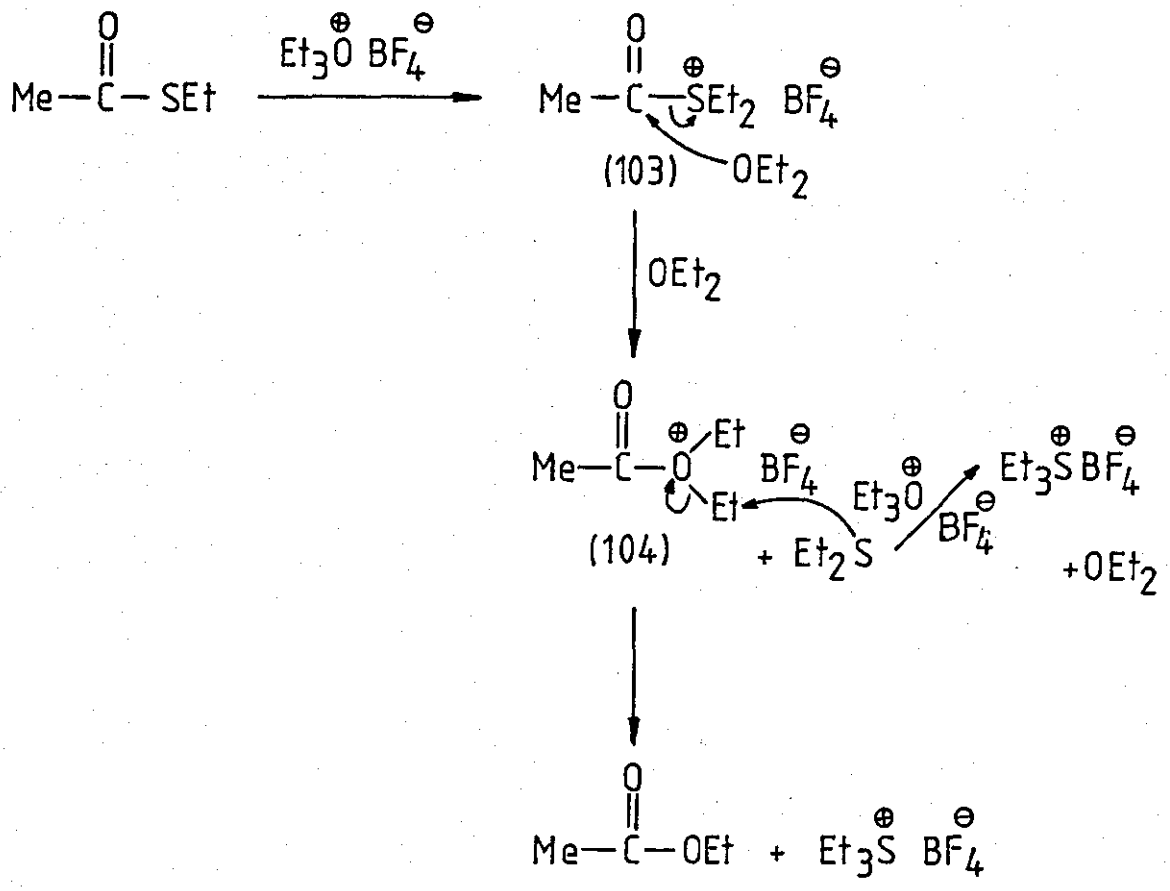
After 18 hours at room temperature the starting materials can still be seen in the ^{13}C nmr spectrum, although peaks at 68.4, 14.1 ppm (diethyl ether/BF_3 complex) and 32.8, 8.5 ppm (triethylsulphonium tetrafluoroborate) are becoming obvious. After 24 hours at room temperature, peaks at 61.4, 20.5 and 14.7 ppm can clearly be seen which are attributable to ethyl acetate (lit.[139] ^{13}C nmr = 171.6; 61.0; 20.5; 14.0 ppm). The mechanism of formation is discussed below.

After 9 days at room temperature the solution is red in colour and exhibits peaks as shown below.



1.not seen.	3.14·7	1.32·7	1.69·2
2.61·6	4.20·7	2.8·5	2.13·6

There is no evidence for alkylation having taken place on the carbonyl oxygen. The products formed can be explained by the following reaction scheme:



The reaction of S-ethyl thioacetate with triethyloxonium tetrafluoroborate to give the S-alkylated product (103) is not unexpected. However this product is not seen in the nmr spectrum as the ether released in the reaction can attack (103) giving the oxonium salt (104) and free diethyl sulphide. Once again the salt (104) is not seen in the spectrum as the diethyl sulphide dealkylates the salt to give ethyl acetate and triethylsulphonium tetrafluoroborate. As there is a slight excess of the triethyloxonium salt present, the triethylsulphonium salt could also be formed by alkylation of the diethyl sulphide formed in the reaction of diethylether with salt (103). The presence of the triethylsulphonium salt confirms that the salt (103) is formed in this reaction as there is no other route by which it could be formed.

The peaks at 69.2 and 13.6 ppm are due to the presence of the diethyl ether/boron trifluoride complex. These peaks are prominent in

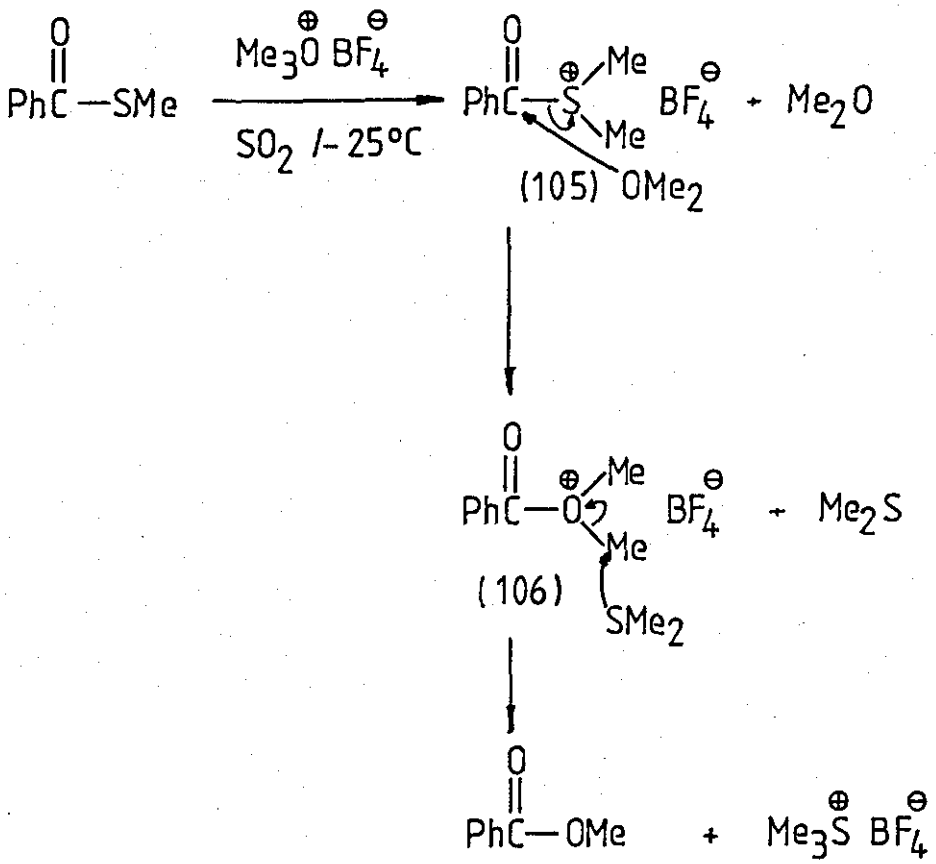
the spectrum, but are due mainly to the breakdown of triethyloxonium tetrafluoroborate[12] rather than as a by-product from the reaction described above.

No further alkylations were attempted.

3.2.7.2 Alkylation of S-methyl thiobenzoate

Methylation using trimethyloxonium tetrafluoroborate gave the results shown in table 5. ^{13}C Nmr shows that very little reaction has taken place after 7 days at -25°C.

Indeed the only noticeable difference between this spectrum and those of the starting materials is a small peak at 26.2 ppm, which is due to the presence of the trimethylsulphonium salt. This is presumably formed by the route shown below, although no peaks can be seen for the other expected product i.e. methyl benzoate.



Thus it can be deduced that the salt (105) is formed in the reaction, but that it is attacked by the dimethyl ether to give (106), which is then dealkylated by the "free" dimethyl sulphide to give methyl benzoate and trimethylsulphonium tetrafluoroborate.

It is expected that reaction at a higher temperature would yield these products in greater yields, but no further work was carried out.

No reactions were carried out using more reactive methylating agents such as methyl triflate, methyl fluorosulphate, dimethoxy-carbenium salts or dimethylhalonium salts. Reactions of these latter three would be expected to give good yields of (105) as there would be no nucleophile present to decompose the salt after its formation.

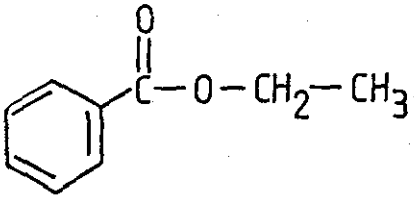
3.2.7.3 Alkylation of S-ethyl thiobenzoate

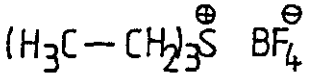
Ethylation using triethyloxonium tetrafluoroborate gave the results shown in table 5. The reaction does not go to completion under these conditions.

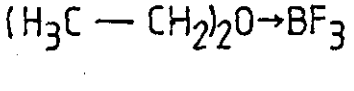
After 15 hours very little reaction has taken place, with the peaks for the starting materials being prominent in the ^{13}C nmr spectrum. The same appeared to be so after 24 hours.

After 4 days at room temperature new peaks are seen at 165.1, 70.0, 61.1, 33.0, 14.6, 13.4 and 8.6 ppm. The peaks in the aromatic region are more numerous and complicated.

After 10 days these new peaks have increased in intensity compared with the starting materials and are attributable to the products shown below.

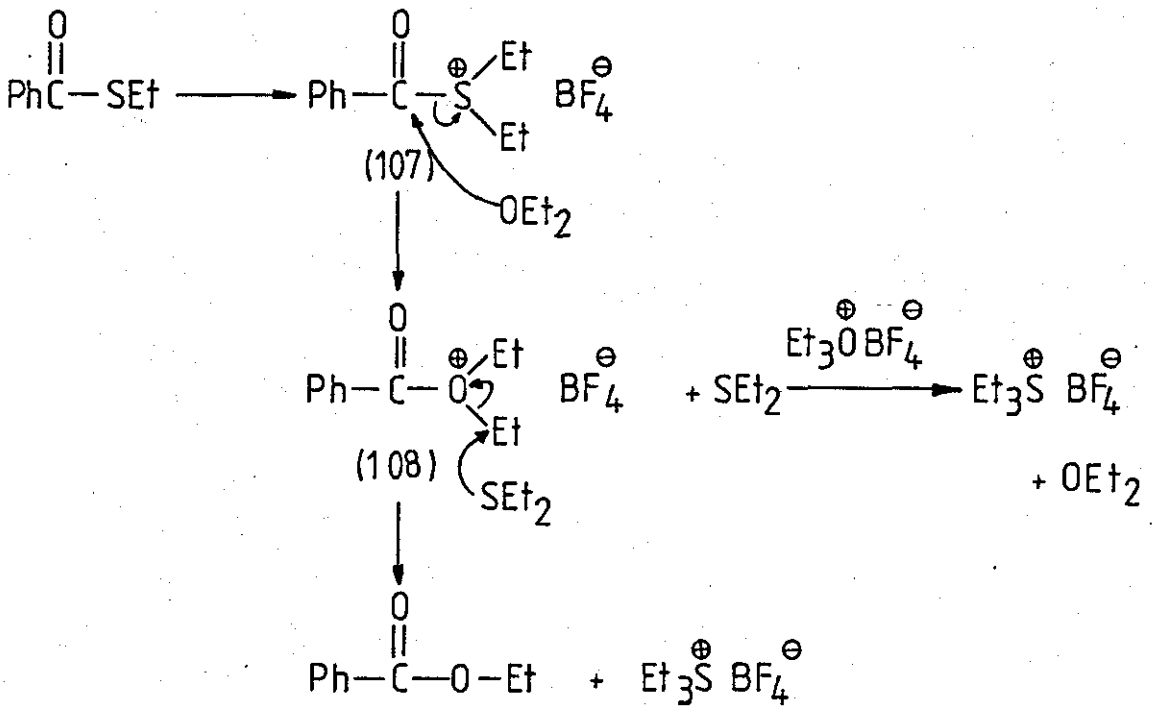






There is no evidence for alkylation on the carbonyl oxygen in this reaction.

These products are formed by the route shown in the scheme below.



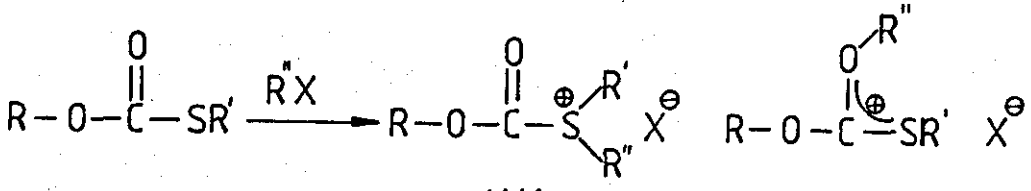
No spectra for (107) and (108) were recorded, but they must have been formed as intermediates to account for the products observed. The peaks at 165.1, 61.1 and 14.6 ppm that have been assigned to ethyl benzoate compare well with the literature values for this material (lit.[140] ^{13}C nmr = 166.3; 60.8; 14.4; 130.9; 129.7; 128.4; 132.8), although assignment of the aromatic carbons proved impossible as the peaks were too numerous and complicated. The peaks at 70.0 and 13.4 ppm are due to the diethyl ether/boron trifluoride complex and are explained by the breakdown of triethyloxonium tetrafluoroborate in solution at room temperature, rather than the reaction above.

No further reactions were attempted although it is felt that further investigations using alkylating agents such as ethyl fluoro/

chlorosulphate, diethoxyarbenium salts and dialkylhalonium salts could be fruitful.

3.2.8 Reaction of thiocarbonic acid esters with alkylating agents

There appear to be no reports of such alkylation reactions in the literature. By drawing analogies with S-alkyl thiocarboxylic acid esters we would expect alkylation to be predominantly on the sulphur atom with possibly slight alkylation on the carbonyl oxygen.



(11) (109)

major product ? minor product ?

The salts (11) and (109) would be expected to undergo the same sort of reactions as their thiocarboxylic acid counterparts (see section 3.2.7). No salts of this type have been reported before.

We decided to investigate this type of reaction using ^{13}C nmr techniques. The reactions were carried out in nmr tubes sealed with a rubber septum to ensure that moisture was excluded from the reaction.

3.2.8.1 Alkylation of S-ethyl O-phenyl thiocarbonate

Ethylation using triethyloxonium tetrafluoroborate gave the results shown in table 6. ^{13}C Nmr shows the presence of several products and these are discussed below. The reaction does not go to completion under these conditions.

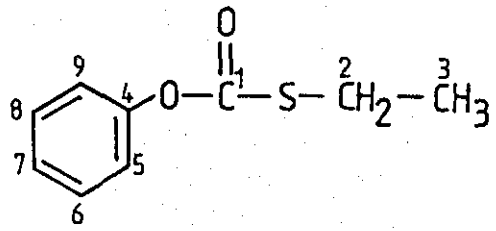
After 12 hours only the starting materials are seen in the ^{13}C nmr spectrum. After 36 hours several other new peaks can be seen, which continue to grow in intensity with the increase in reaction time. The results described below were achieved after 5 days at room temperature.

After 5 days the major product is the S-alkylated product (110) which seems to be stable under our reaction conditions. This

Table 6

6.

Thiol Carbonate



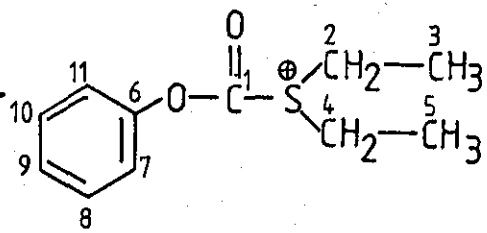
1. 170.2 ppm
2. 25.6
3. 14.8
4. 151.4
5. 121.4
6. 129.5
7. 126.1
8. 129.5
9. 121.4

Conditions[a]

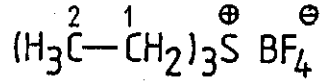
$Et_3\overset{\oplus}{O}\ \overset{\ominus}{BF_4}$

CD_2Cl_2, rt.

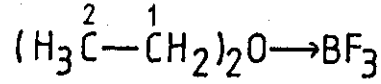
Products



1. 153.9 ppm
2. 36.5
3. 9.9
4. 36.5
5. 9.9
6. 151.6
7. 120.8
8. 130.5
9. 128.7
10. 130.5
11. 120.8

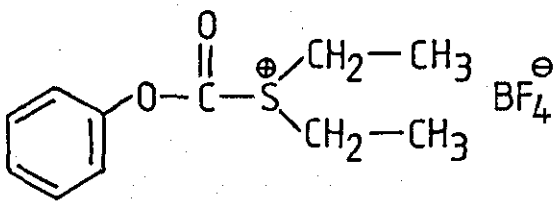


1. 32.8 ppm
2. 8.6

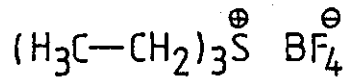


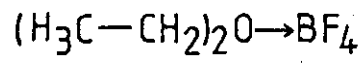
1. 69.0 ppm
2. 13.9

(a) See experimental for full details.



(110)





stability is not too surprising as this type of salt is also isolated when phenyl chloroformate and diethyl sulphide are allowed to react together in sulphur dioxide in the presence of antimony pentachloride (see section 3.2.2.2), and appears to be reasonably stable to nucleophilic attack by the excess diethyl sulphide present. There is no evidence for the formation of an O-alkylated product.

The carbonyl carbon in salt (110) has moved upfield by 16.3 ppm compared with the starting material, which reflects the presence of the positive charge on the adjacent sulphur atom. The methylene and methyl carbon shifts have also changed significantly. The methylene carbons next to the sulphur atom in (110) have moved downfield by 10.9 ppm compared with the thiocarbonate, whereas the methyl carbons have moved upfield by 4.9 ppm. These two values should be compared with those for the triethylsulphonium salt (32.8, 8.6 ppm) where the positive charge is stabilised by three ethyl groups rather than two as in salt (110) (36.5, 9.9 ppm). The aromatic carbon shifts have not changed significantly, the quaternary, meta-, and para-carbons having moved downfield by 0.2, 1.0 and 2.6 ppm respectively, and the ortho-carbon upfield by 0.6 ppm.

There is evidence that the salt (110) is attacked by the liberated ether to give ethyl phenyl carbonate and triethylsulphonium tetrafluoroborate in the same manner as seen in the alkylation of S-alkyl thiocarboxylic acids using trialkyloxonium tetrafluoroborates (see section 3.2.7). However, this reaction seems to be a minor reaction compared with the main alkylation reaction as the ^{13}C nmr peaks are only just discernible in the spectrum. The peaks at 69.0 and 13.9 ppm are due to the diethyl ether/boron trifluoride complex

formed by decomposition of triethyloxonium tetrafluoroborate in solution[12].

No further reactions were carried out on this system. It is felt however, that alkylation using other alkylating agents that do not produce nucleophilic by-products would yield these salts in good yield and purity. Further investigation is needed to determine their value in organic synthesis.

3.2.9 Vacuum-line techniques

The vacuum-line system is described fully in section 3.3.9, together with details of the techniques used to carry out many of the reactions discussed in the previous sections (3.2.1-3.2.8).

The system was designed to facilitate the carrying out of reactions under anhydrous conditions.

Reagents such as antimony pentachloride and antimony pentafluoride are difficult to handle even in a dry-box purged with an inert gas. A vacuum-line enables them to be readily distilled into the reaction at a controlled rate and in a given quantity (see hanging burette).

In the ideal system, the products can be isolated without removal from the vacuum line. This was not possible in all our experiments.

3.3 Experimental

The general experimental details as laid out in section 2.3 apply.

The yields are based on the total mass of starting materials used in the reaction, unless otherwise stated i.e. 75% = 75% of material recovered as product(s).

Where possible the identity of the product was verified by comparison of the spectral details with those of an authentic sample.

These results are discussed in detail in sections 3.2.1 to 3.2.8 above.

3.3.1 Reaction of chloroformates with sulphides

3.3.1.1 Reaction of phenyl chloroformate with dimethyl sulphide

Dimethyl sulphide (0.0268g, 0.43 mmole) was added to a solution of phenyl chloroformate (0.0684g, 0.43 mmole) in liquid sulphur dioxide (∿ 0.3 cm^3) at -60°C in an nmr tube sealed with a rubber septum. d_2-Methylene chloride (0.2 cm^3) was added and the tube was stored at -15°C. ^{13}C Nmr analysis at -20°C after 8 days showed no reaction had taken place, the starting materials only being present.

^{13}C nmr ppm (CD_2Cl_2/SO_2) 17.1; 146.7; 151.7; 121.0; 130.4; 127.9; (lit.:- phenyl chloroformate[123]: 149.3; 151.8; 120.5; 129.9; 127.2; dimethyl sulphide[129] 19.3).

3.3.2 Reaction of chloroformates with sulphides in the presence of a Lewis acid

These reactions were carried out using the two experimental techniques described below.

Method A

The apparatus is described in Chapter 2, section 2.3.2. Antimony pentachloride (2.99g, 0.01 mole) was added to methylene chloride (5 cm^3) at -70°C. To this was added the sulphide (0.01 mole) which gave an orange colouration often accompanied by some pale yellow solid. The solution was left to stand for 30 minutes at -70°C. The chloroformate (0.01 mole) was then added with swirling, and left at -70°C for 1 hour. The reaction was then warmed to approximately -25°C and left for 7 days. After this time the reaction was cooled to -70°C and the solid was isolated by filtration. The pale yellow solid was washed with cold methylene chloride (2 x 10 cm^3) and dried under vacuum at room temperature. The yields are given below, together with spectral details of the products.

Method B

These reactions were carried out in an nmr tube equipped with a rubber septum so that the reactants could be injected in thus ensuring anhydrous conditions. Sulphur dioxide (approx. 0.2 cm^3) was distilled in and to this was added, at -60°C, the chloroformate (0.4 mmole).

Antimony pentachloride (0.5 mmole) was added to give a clear, almost colourless solution. After 30 minutes at this temperature the sulphide (0.4 mmole) was added, followed by a small amount of d_2-methylene chloride (0.2 cm^3). The nmr spectra were run after 24 hours at -20°C. The results are given below.

3.3.2.1 Reaction of phenyl chloroformate with dimethyl sulphide in the presence of antimony pentachloride

This reaction was studied using both methods given above.

(a) Using Method A - A cream-coloured solid was formed in 43% yield, which was hydroscopic. No melting point could be taken.

IR (C=O) in CH_3CN 1798 cm^{-1}.
^1H nmr δ (SO_2/CD_2Cl_2) at -20°C 3.13 (s); 3.19 (s); 7.55-8.45 (m).
^{13}C nmr ppm (SO_2/CD_2Cl_2) at -20°C 14.1; 27.2; 29.7; 34.9; 113.6; 118.6; 121.1; 122.1; 127.5; 128.2; 130.6; 132.4; 161.2.

(b) Using Method B - A clear, yellow solution was seen at -15°C, with no suspended solid.

^1H nmr δ (SO_2/CD_2Cl_2) at -15°C 2.69 (v. broad s); 3.00 (s); 3.21 (s); 3.33 (s); 3.47 (s); 7.10-7.80 (m).
^{13}C nmr ppm (SO_2/CD_2Cl_2) at -15°C 23.5 (broad); 25.5; 30.0; 35.5; 120.1; 121.0; 128.1; 129.2; 130.6; 130.9; 132.3; 151.4.

These results are discussed in detail in section 3.2.2.1.

3.3.2.2 Reaction of phenyl chloroformate with diethyl sulphide in the presence of antimony pentachloride

This reaction was studied using both methods given above.

(a) Using Method A - A pale yellow solid was isolated in 11% yield.

^{13}C nmr ppm (SO_2/CD_2Cl_2) at -20°C 7.0; 42.7.

(b) Using Method B - A clear, yellow solution was formed at -20°C.

^1H nmr δ (SO_2/CD_2Cl_2) at -20°C 1.52 (t, 6H; 3.38 (2 x q, 4H); 3.79 (broad q); 7.17-7.65 (m, 5H).
^{13}C nmr ppm (SO_2/CD_2Cl_2) at -20°C 8.5; 9.3; 10.0; 10.7; 32.4; 35.9; 36.7; 39.4; 118.7; 120.1; 120.9; 127.9; 129.0; 130.4; 130.8; 133.5; 150.4; 151.3; 161.5.

These results are discussed in detail in section 3.2.2.2.

3.3.2.3 Reaction of phenyl chloroformate with tetrahydrothiophene in the presence of antimony pentachloride

This reaction was studied using Method A above. Addition of tetrahydrothiophene to the Lewis acid gave a voluminous cream solid which was insoluble in methylene chloride. On adding phenyl chloroformate the solution became bright yellow, but the solid remained. A bright yellow solid was isolated in 66% yield, and seemed to be hygroscopic. No melting point could be obtained. Dissolution in d_3-acetonitrile gave a clear yellow solution.

IR (C=O) in CH_3CN 1784 cm^{-1}.

^1H nmr δ (CD_3CN) 1.30-2.55 (broad m); 2.55-3.95 (broad m); 6.45-7.65 (broad m).

^{13}C nmr ppm (CD_3CN) 29.6 (broad m); 31.1 (broad m); 36.3 (broad m); 44.4 (broad m); 121.3; 128.2; 130.8; 133.3; 150.4; 152.4.

3.3.3 Reaction of chloroformates with sulphides in the presence of silver hexafluoroantimonate

The three general procedures described below were used in these investigations. The silver salt was dried over P_2O_5 in a vacuum (0.3 mm Hg) for several days before use.

Method A

A 50 cm^3 round-bottomed flask equipped with rubber septum was used in these reactions. The silver hexafluoroantimonate (2.5 mmole) was added to the flask in a dry-box under a nitrogen atmosphere. To this was added methylene chloride (25 cm^3) to give a clear solution. The sulphide (2.5 mmole/5 mmole (see results and discussion)) was added to this at room temperature, which generally gave a small amount of colourless solid. The flask was removed from the dry-box and cooled to -25°C. The chloroformate (2.5 mmole) was dissolved in methylene chloride (approx. 2 cm^3) and added over a 15 minute period. The reaction was allowed to warm slowly to room temperature, and was then stirred for 22 hours at this temperature. The solid was then filtered

off and the filtrate was evaporated down to give a viscous liquid generally. These products were analysed using IR and nmr techniques and the results are given below.

Method B

The reactions were carried out in a sealed tube to ensure exclusion of moisture. The dried silver hexafluoroantimonate (2.2 mmole) was placed in the tube and methylene chloride (approx. 3 cm^3) was added. To this was added the sulphide (4.4 mmole) and the mixture was rapidly cooled to -40°C. The chloroformate (2.2 mmole) was added, and the tube was sealed using a torch. The reaction was allowed to warm to approx. -25°C. After 24 hours at this temperature some colourless solid had generally formed. After 2 days at -25°C the reaction was warmed to room temperature and left to stand for a further 3 days. After this time the ampoule was opened, the solid was filtered off and the solvent was evaporated from the filtrate to yield a very pale yellow, viscous fluid. These products were analysed as in Method A above.

Method C

The reaction was carried out on the vacuum-line using the general techniques described in section 3.3.9. The silver salt (1.7 mmole) was pumped at less than 0.1 mm Hg for 18 hours before use. Methylene chloride (15 cm^3) was distilled in to give a clear solution at -60°C. The chloroformate (1.6 mmole) was then distilled in and the flask was warmed to -60°C and the contents were stirred at this temperature for 30 minutes. The sulphide (3.2 mmole) was distilled in and the reaction was stirred for 30 minutes before being allowed to come slowly to room temperature. The reaction mixture was stirred for a further 3 days at room temperature. The flask was detached from the vacuum-line and worked up as in Method A above. The results are given below.

3.3.3.1 Reaction of phenyl chloroformate with dimethyl sulphide in the presence of silver hexafluoroantimonate

This reaction was studied using the three methods described above.

(a) Using Method A - Two experiments were carried out, one using equimolar amounts of reactants, the other using two molar equivalents of the sulphide.

(i) With equimolar quantities - The solid isolated initially was dissolved in methylene chloride (5 cm^3), filtered, and ether was added until colourless crystals were formed. These were filtered off. Yield = 32%, colourless crystals.

^1H nmr δ (CD_2Cl_2) 2.50 (s).
^{13}C nmr ppm (CD_2Cl_2) 21.1.

The initial filtrate was evaporated down to yield an orange oil with a small amount of crystalline product. Yield = 56%.

IR (C=O) 1787, 1728 cm^{-1}; (O-H) 3000-3700 cm^{-1} (broad).
^1H nmr δ ($CDCl_3$) 2.38 (s); 2.57 (s); 6.60-7.50 (m); 8.60 (s, exchangeable with D_2O).
No ^{13}C nmr spectrum was run.

(ii) With two equivalents of dimethyl sulphide - Using the same procedure as in (i) above, colourless cyrstals were isolated in 46% yield.

^1H nmr δ (CD_2Cl_2) 2.51 (s).
No ^{13}C nmr spectrum was run.

The initial filtrate yielded a colourless, sticky mass. This was washed with chloroform to yield a clear, yellow oil in 15% yield.

IR (C=O) 1787, 1729 cm^{-1}; (O-H) 3100-3600 cm^{-1} (broad).
^1H nmr δ ($CDCl_3$) 2.37 (s); 6.52-7.70 (m).
No ^{13}C nmr spectrum was run.

(b) Using Method B - A grey solid was isolated in 58% yield. This solid became darker on exposure to light.

^1H nmr δ (CD_2Cl_2) 2.94 (s).
No ^{13}C nmr spectrum was run.

The filtrate gave a yellow, viscous oil in 32% yield.

IR (C=O) 1728 cm^{-1}; (O-H) 3150-3600 cm^{-1} (broad).
'H nmr δ ($CDCl_3$) 2.39 (s); 6.75-7.55 (m).

(c) Using Method C - A dark grey solid was isolated in 55% yield.

'H nmr δ (D_2O) 2.82 (s).
No ^{13}C nmr spectrum run.

Addition of ether to the filtrate gave a further amount of colourless solid. Yield = 7%.

'H nmr δ ($CDCl_3$) 2.50 (s).
No ^{13}C nmr spectrum run.

The filtrate was evaporated down to give an orange oil in 24% yield. Flask to flask distillation on the vacuum-line gave a clear, colourless oil in 20% yield overall, but an 83% yield based on the expected amount of S-methyl O-phenyl thiocarbonate.

IR (C=O) 1728 cm^{-1}
'H nmr δ ($CDCl_3$) 2.37 (s, 3H); 6.95-7.45 (m, 5H).
^{13}C nmr ppm ($CDCl_3$) 13.6; 151.5; 121.4; 129.6; 126.2; 170.8.

These results are discussed fully in section 3.2.3.1.

3.3.3.2 Reaction of phenyl chloroformate with dibenzyl sulphide in the presence of silver hexafluoroantimonate

The reaction was studied using Method A above with two molar equivalents of the sulphide. No solid was formed initially. The solution was evaporated down to give an orange, sticky mass, which was taken up in methylene chloride (20 cm^3). To this was added ether whereupon large needles crystallised out. These were filtered off. Yield = 65% colourless needles that darkened on standing in the light.

'H nmr δ ($CDCl_3/CD_2Cl_2$) 3.89 (s, 4H); 7.22 (s, 10H).
No ^{13}C nmr spectrum was run.

The filtrate was evaporated down to give a yellow oil in 15% yield. Gas chromatography showed this to be essentially unreacted phenyl chloroformate, with a small amount of phenol.

IR (C=O) 1788 cm^{-1}; (O-H) 3150-3650 cm^{-1}.

^1H nmr δ ($CDCl_3$) 6.95-7.50 (m).

No ^{13}C nmr spectrum was run.

3.3.3.3 Reaction of methyl chloroformate with dimethyl sulphide in the presence of silver hexafluoroantimonate

The reaction was studied using Method A with equimolar quantities of reactants. Very little solid was formed during the reaction. The reaction mixture was evaporated down to yield a sticky, grey, crystalline mass. This was dissolved in dichloromethane (20 cm^3) and ether was added until fine colourless needles were formed. These were filtered off. Yield = 69%, fine colourless needles.

^1H nmr δ (CD_2Cl_2) 2.47 (s).

^{13}C nmr ppm (D_2O) 19.8; 20.8.

(CD_2Cl_2) 21.1.

The filtrate was evaporated down to give a small amount of colourless crystals that had similar spectra to the product already mentioned.

3.3.3.4 Reaction of ethyl chloroformate with dimethyl sulphide in the presence of silver hexafluoroantimonate

The reaction was carried out according to Method A above. There was little initial solid formation so the solvent was evaporated to yield a colourless solid. This was taken up in methylene chloride (20 cm^3), filtered (insoluble silver halide) and ether was added until colourless needles came out of solution. These were filtered off. Yield = 61%, fine colourless needles.

^1H nmr δ (CD_2Cl_2) 2.49 (s).

^{13}C nmr ppm (D_2O) 20.9.

The filtrate was evaporated to give a small amount of colourless solid (15% yield) which appeared to be identical with the product above.

3.3.4 Reaction of acyl halides with sulphides

3.3.4.1 Reaction of benzoyl chloride with dimethyl sulphide

Benzoyl chloride (0.0606g, 0.43 mmole) was added to a solution of dimethyl sulphide (0.0268g, 0.43 mmole) in liquid sulphur dioxide (approx. 0.3 cm^3) at -60°C in an nmr tube sealed with a rubber septum. d_2-Methylene chloride (0.2 cm^3) was added and the tube was stored at -15°C. ^{13}C Nmr analysis at -20°C after 8 days revealed that no reaction had taken place.

^{13}C nmr ppm (CD_2Cl_2/SO_2) 17.0; 167.9; 133.4; 131.9; 129.6; 136.3. (lit.:- benzoyl chloride[131]: 168.0; 133.1; 131.3; 128.9; 135.3. Dimethyl sulphide[129] 19.3).

3.3.5 Reaction of acyl halides with sulphides in the presence of a Lewis acid

These reactions were carried out using one or more of the following experimental procedures.

Method A

The apparatus is described in Chapter 2, section 2.3.2. The acyl halide (8.6 mmole) was added to a pre-cooled solution of the Lewis acid (8.6 mmole) in liquid sulphur dioxide (approx. 5 cm^3) at -50°C. The sulphide (8.6 mmole or 10 times excess) was then added maintaining the temperature at -50°C. The reaction was left for 6 hours at -15°C and was then allowed to come slowly to room temperature under a dry nitrogen atmosphere. After 1 day at room temperature the sulphur dioxide had evaporated to yield a cream solid. This was washed with ether (2 x 5 cm^3) and dried under vacuum. The filtrate was evaporated down to yield a viscous oil. These products and their yields are described below, and were characterised using IR and nmr techniques.

Method B

The apparatus was as in Method A above. Antimony pentachloride (10 mmole) was added which usually gave an orange/yellow solid at -70°C. This was left to stand at -70°C for 30 minutes, after which time the acyl halide (10 mmole) was added. The reaction was left at -70°C for 1 hour

and then allowed to warm to 0°C over a period of 5 hours. After standing at room temperature overnight the reaction was cooled to -70°C, the solvent was filtered off, and the solid was washed with methylene chloride (2 x 5 cm^3) at -70°C. The solid was then dried under vacuum at -50°C for 3 hours and then at room temperature for 12 hours. The solid was characterised using nmr techniques, and the results are given below.

Method C

The apparatus was as in Method A. The procedure was as in Method B above except that the acyl halide was added to the Lewis acid solution before the sulphide was added. The results are given below.

Method D

The reaction was carried out in an nmr tube. To a solution of the Lewis acid (0.46 mmole) in sulphur dioxide (approx. 0.2 cm^3) at -60°C was added the acyl halide (0.43 mmole). This was shaken to ensure thorough mixing, and then left for 1 hour at this temperature. The sulphide was then added, followed by d_2-methylene chloride (0.2 cm^3), and the nmr spectra were run immediately. The results are given below.

Method E

The reaction was carried out as in Method D except that the nmr tube was attached to a vacuum-line and all reagents were distilled directly into the tube to ensure anhydrous conditions. This enabled antimony pentafluoride to be used in place of antimony pentachloride. It also enabled sulphuryl chloride fluoride to be used as a solvent. The results are given below.

3.3.5.1 Reaction of benzoyl chloride with dimethyl sulphide in the presence of antimony pentachloride

This reaction was studied using three of the general methods described above.

(a) Using Method A - Addition of the benzoyl chloride to the solution of antimony pentachloride in liquid sulphur dioxide gave a large amount

of solid at -50°C, which disappeared when the dimethyl sulphide (10 x excess) was added, giving an orange solution. After 6 hours at -50°C, the sulphur dioxide was allowed to evaporate to give a white solid. This was washed with ether (10 cm^3). Yield = 34%, white solid (87% of theoretical yield for $Me_3\overset{+}{S}\ SbCl_6^-$).

^1H nmr δ (D_2O) 2.87 (s).

The filtrate was evaporated down to give a brown, tarry residue in 10% yield (62% of theoretical yield for S-methyl thiobenzoate).

^1H nmr σ ($CDCl_3$) 2.42 (broad s); 7.20-7.75 (m); 7.85-8.25 (m); 11.12 (s).
No ^{13}C nmr spectrum was run.

(b) Using Method B - Addition of dimethyl sulphide to the solution of antimony pentachloride in methylene chloride gave a bulky pale yellow solid at -70°C. On adding the benzoyl chloride little change was seen. The cream solid was isolated in 38% yield.

IR (C=O) in CH_3CN 1775 cm^{-1}.
^1H nmr δ (SO_2/CD_2Cl_2) at -20°C 2.89 (s); 3.07 (broad s); 7.35-8.25 (m).
^{13}C nmr ppm (SO_2/CD_2Cl_2) at -20°C 27.4; 35.8; 129.4; 129.7; 130.6; many aromatic carbons not assignable; carbonyl carbon not seen.

(c) Using Method D - On mixing benzoyl chloride with antimony pentachloride in liquid sulphur dioxide at -60°C an immediate cream-coloured precipitate was formed. When dimethyl sulphide was added the solution became clear and yellow.

^{13}C nmr ppm (SO_2/CD_2Cl_2) at -20°C 22.1 (broad); 128.9; 129.2; 129.6; 130.5; 131.3; 131.8; 132.5; 132.7; 134.9; 136.5; 140.0; 167.6.

3.3.5.2 Reaction of benzoyl chloride with diethyl sulphide in the presence of antimony pentachloride

Using Method A - Addition of benzoyl chloride to the solution of antimony pentachloride in liquid sulphur dioxide at -60°C gave a pale yellow solid, which went quickly into solution when the diethyl sulphide (10 x excess) was added. After 2 hours at this temperature the flask was

allowed to come to room temperature and the sulphur dioxide was evaporated off. This gave a dark brown liquid in 38% yield. This was washed with ether (approx. 2 x 5 cm^3) and the filtrate was evaporated down to yield a brown oil.

IR (C=O) 1774, 1722, 1684, 1665 cm^{-1}.
^1H nmr δ ($CDCl_3$) 1.28 (5); 2.55 (broad q); 7.25-7.60 (m); 7.65-8.20 (m).

3.3.5.3 Reaction of benzoyl chloride with diphenyl sulphide in the presence of antimony pentachloride

No experimental work was carried out on this reaction.

3.3.5.4 Reaction of benzoyl chloride with tetrahydrothiophene in the presence of antimony pentachloride

Using Method C above a yellow solid was isolated in 62% yield. Attempts to dissolve this solid in methylene chloride, chloroform and liquid sulphur dioxide failed. No nmr spectra were obtained. The solid seemed to partially liquefy at room temperature - no melting point could be obtained.

Similar results were obtained using Methods B and D.

3.3.5.5 Reaction of acetyl chloride with dimethyl sulphide in the presence of antimony pentachloride

The reaction was studied using Method B above. This gave a pale yellow solid in 37% yield. No melting point could be taken.

^1H nmr δ (SO_2/CD_2Cl_2) at -20°C 2.85 (s); 3.23 (s); 3.48 (broad s).
^{13}C nmr ppm (SO_2/CD_2Cl_2) at -10°C 27.2; 35.7.

3.3.5.6 Reaction of acetyl chloride with diethyl sulphide in the presence of antimony pentachloride

Reaction using Method B above gave no solid product. Addition of chloroform failed to give a precipitate. The reaction was not investigated further, and no spectra were recorded.

3.3.5.7 Reaction of benzoyl fluoride with dimethyl sulphide in the presence of antimony pentafluoride

Reaction according to Method E above using sulphuryl chloride fluoride as the solvent, gave a bulky colourless precipitate at -60°C, that dissolved to give a clear, colourless solution at -50°C. This was left for 1 hour at -50°C before the nmr spectrum was run.

^{1}H nmr δ (SO_2ClF/CD_2Cl_2) at -20°C 2.24 (broad s); 2.45 (s); 2.88 (s); 3.11 (v. broad s); 7.35-7.80 (m); 7.90-8.15 (m).

^{13}C nmr ppm (SO_2ClF/CD_2Cl_2) at -20°C 88.6; 132.7; 141.6; 148.6; 153.9 (no aliphatic carbons could be seen).

3.3.6 Reaction of acyl halides with sulphides in the presence of silver hexafluoroantimonate

These reactions were carried out using one or more of the following procedures. The silver salt was dried as in section 3.3.3.

Method A

The apparatus was as in section 3.3.3, Method A. The silver salt (3.2 mmole) was added to the flask in a dry-box under a nitrogen atmosphere. Methylene chloride (25 cm^3) was added to give a clear solution. The sulphide (3.1 mmole/6.4 mmole (see results and discussion)) was added at room temperature which gave a slight cloudiness. The flask was removed from the dry-box and cooled to approx. -25°C with stirring. The acyl halide (3.1 mmole) was added over a 15 minute period, and the reaction was stirred at -25°C for 30 minutes before being allowed to warm to room temperature. The reaction was stirred for 24 hours at room temperature. After this time the solid was filtered off. The solvent was evaporated from the filtrate to yield a semi-crystalline mass.

These products and their yields are reported below, together with their nmr and IR spectral data.

Method B

The reaction was carried out in a sealed tube. The silver salt (2.2 mmole) was placed in the tube and methylene chloride (5 cm^3) was

added. The sulphide (4.4 mmole) was added to this and the mixture was cooled to -50°C. The acyl halide (2.2 mmole) was added, and the tube was sealed using a torch. The reaction was warmed to -25°C for 48 hours, and was then allowed to stand at room temperature for 3 days. The tube was opened, the solid was filtered off and was washed with methylene chloride (3 x 5 cm^3) to give a colourless precipitate. The solvent was evaporated from the initial filtrate to give a pale yellow, sticky solid. These products were analysed as in Method A above.

Method C

The reaction was carried out on the vacuum-line using the general techniques described in section 3.3.9 and the apparatus shown in section 3.3.3, Method C. The silver salt (1.7 mmole) was pumped down at less than 0.1 mm Hg for 12 hours before use. Methylene chloride (25 cm^3) was distilled in followed by the acyl halide (1.7 mmole). On warming to -70°C a bulky, colourless precipitate was formed, which was stirred for 45 minutes. The sulphide (3.1 mmole) was distilled in, stirred for 30 minutes at -50°C, and then the reaction was allowed to warm slowly to room temperature. The reaction mixture was stirred for a further 3 days at room temperature. The flask was then detached from the line and was worked up as in Method A above. The products and yields are given below together with their spectral data.

3.3.6.1 Reaction of benzoyl chloride with dimethyl sulphide in the presence of silver hexafluoroantimonate

This reaction was studied using all three of the procedures described above.

(a) Using Method A - Two experiments were carried out, one using equimolar amounts of reactants, the other using two molar equivalents of the sulphide.

(i) With equimolar quantities - The initially formed solid was filtered off. Yield = 27%, colourless solid. No analysis was carried out on this solid. The filtrate was evaporated down to give a colourless crystalline mass. Yield = 40%.

^{1}H nmr δ ($CDCl_3$) 2.47 (s); 7.30-7.70 (m); 7.90-8.25 (m); 9.40 (broad s, exchanges with D_2O).

(ii) With two equivalents of dimethyl sulphide - Little solid seemed to have been formed in the reaction, so ether (approx. 25 cm^3) was added. This gave a colourless crystalline product which was filtered off. Yield = 50%, colourless crystals that turned grey on exposure to light.

^{1}H nmr δ (CD_2Cl_2) 2.51 (s).
^{13}C nmr ppm (D_2O) 20.7.

The filtrate was evaporated down to give a colourless cyrstalline solid. Yield = 21%.

IR (C=O) 1685 cm^{-1}; (O-H) 2500-3700 cm^{-1}.
^{1}H nmr δ ($CDCl_3$) 2.47 (s); 7.25-7.70 (m); 7.85-8.20 (m).

(b) Using Method B - The initial solid was filtered off. Yield = 36%, colourless solid that became grey on exposure to light. No spectra were run on this solid. The filtrate was evaporated down to give a sticky, pale yellow solid. Yield = 35%.

No IR spectrum was run.
^{1}H nmr δ ($CDCl_3$) 2.38 (s); 2.48 (s); 7.25-7.65 (m); 7.80-8.20 (m).

(c) Using Method C - Two experiments were carried out, one using two molar equivalents of dimethyl sulphide, the other using a ten molar excess of the sulphide.

(i) With two equivalents of dimethyl sulphide - The initially formed colourless solid was filtered off. Yield = 9%, solid darkened on exposure to light. The filtrate was evaporated down to yield a pale yellow solid. This was taken up in methylene chloride (5 cm^3) and ether was added (20 cm^3) to give a crystalline solid. This was filtered off. Yield = 34%, pale yellow crystals.

^{1}H nmr δ ($CDCl_3$) 2.47 (s).
No ^{13}C nmr spectrum was run.

The filtrate was evaporated down to give a sweet-smelling, yellow

solid. Yield = 53%. No melting point could be taken.

IR (C=O) in $CHCl_3$ 1665 (sh); 1685 (st, broad) cm^{-1}; (O-H) 2400-3600 cm^{-1}.

'H nmr δ ($CDCl_3$) 2.39 (s); 2.47 (s); 7.20-7.60 (m); 7.80-8.15 (m); 10.98 (broad s, exchanges with D_2O).

No ^{13}C nmr spectrum was run.

(ii) With excess dimethyl sulphide - The initially formed solid was filtered off. Yield = 46%, grey solid.

'H nmr δ (D_2O) 2.85 (s).

No ^{13}C nmr spectrum was run.

The filtrate was evaporated down to give a yellow, tacky solid. Yield = 31%.

IR (C=O) in $CHCl_3$ 1667 (st), 1685 (st) cm^{-1}; (O-H) 2400-3600 cm^{-1}.

'H nmr δ ($CDCl_3$) 2.44 (s); 7.25-7.60 (m); 7.75-8.15 (m); 12.12 (s, exchanges with D_2O).

3.3.7 Reaction of thiocarboxylic acid esters with alkylating agents

The thiocarboxylic acid esters were prepared according to one of the procedures below (section (a)). The alkylating agents were prepared according to standard procedures (see section 2.3.7(b)).

The alkylations were carried out under anhydrous conditions using one of the procedures given in section 2.3.7(c).

(a) Preparation of thiocarboxylic acid esters

S-Ethyl thioacetate

Prepared from acetyl chloride and ethane thiol according to the method of Baker[141]. Yield = 73%, colourless liquid, b.pt. 116-116.5°C (lit.[141] 116-116.2°C at 749.3 mm).

IR (C=O) 1690 cm^{-1}.

'H nmr δ ($CDCl_3$) 1.22 (t, 3H); 2.29 (s, 3H); 2.85 (q, 2H).

^{13}C nmr ppm ($CDCl_3$) 15.1; 23.5; 30.9; 195.6.

S-Ethyl thiobenzoate

Ethane thiol (5.35g, 0.086 mole) was added dropwise and with stirring to a solution of benzoyl chloride (6.06g, 0.043 mole) and pyridine (3.4g, 0.043 mole) in benzene (100 cm^3, Na-dried), and left to stand for 4 days at room temperature. The pyridine hydrochloride was filtered off, the solution was washed with water (2 x 100 cm^3) and then dried over anhydrous $MgSO_4$. Filtration, and evaporation of the solvent under reduced pressure gave the crude product. Distillation gave pure S-ethyl thiobenzoate in 52% yield, b.pt. 81-82°C at 0.5 mm Hg (lit.[142] 146°C at 31 mm Hg).

IR (C=O) 1662 cm^{-1}.

^1H nmr δ ($CDCl_3$) 1.31 (t, 3H); 3.03 (q, 2H); 7.10-7.70 (m, 3H); 7.75-8.20 (m, 2H).

^{13}C nmr ppm ($CDCl_3$) 14.6; 23.3; 137.3; 127.1; 128.5; 133.1; 192.0.

(b) Alkylation of thiocarboxylic acid esters

The ^{13}C spectral data given below relate only to the alkylated product. Those due to excess starting material or other by-products such as ether, etc., are not shown but are mentioned in the discussion of these reactions.

3.3.7.1 S-Ethyl thioacetate

Ethylated using Method C to give an almost clear solution after 18 hours. Spectra run after 18 hours, 24 hours, and 9 days (red coloured solution).

^{13}C nmr ppm (CD_2Cl_2) O-Alkylation product not seen (see discussion).

3.3.7.2 S-Methyl thiobenzoate

Methylated using Method A to give a clear orange-coloured solution. Spectrum run after 7 days at -25°C.

^{13}C nmr ppm (CD_2Cl_2/SO_2), -20°C O-Alkylation product not seen (see discussion).

3.3.7.3 S-Ethyl thiobenzoate

Ethylated using Method C to give a clear solution after 15 hours. Spectra run after 15 hours, 24 hours, 4 days and 10 days.

^{13}C nmr ppm (CD_2Cl_2) O-Alkylation product not seen (see discussion).

3.3.8 Reaction of thiocarbonic acid esters with alkylating agents

The thiocarbonic acid ester was prepared according to the procedure below (section (a)). The alkylating agent was prepared according to a standard procedure[98] (see section 2.3.7(b)).

The alkylation was carried out under anhydrous conditions using one of the procedures given in section 2.3.7(c).

(a) Preparation of thiocarbonic acid esters

S-Ethyl O-phenyl thiocarbonate

Ethanethiol (7.31g, 0.12 mole) was added dropwise with stirring and cooling to a solution of phenyl chloroformate (16.75g, 0.11 mole) and pyridine (8.64g, 0.11 mole) in toluene (100 cm^3), and left to stand for 3 days at room temperature. The pyridine hydrochloride was filtered off, the solution was washed with water (2 x 100 cm^3) and then dried over anhydrous $MgSO_4$. Filtration, and evaporation of the solvent under reduced pressure gave the crude product. Distillation gave pure thiocarbonate in 51% yield, b.pt. 140-142°C at 200 mm Hg.

IR (C=O) 1728 cm^{-1}.

'H nmr δ ($CDCl_3$) 1.30 (t, 3H); 2.88 (q, 2H); 7.14 (m, 5H).

^{13}C nmr ppm ($CDCl_3$) 14.8; 25.6; 151.4; 121.4; 129.5; 126.1; 170.2.

(b) Alkylation of thiocarbonic acid esters

The ^{13}C spectral data given below relate only to the alkylated product. Those due to excess starting material or other by-products such as ether, etc., are not shown but are mentioned in the discussion of these reactions.

3.3.8.1 S-Ethyl O-phenyl thiocarbonate

Ethylated using Method C to give a clear solution after 12 hours. Spectra run after 12 hours, 36 hours and 5 days.

^{13}C nmr ppm (CD_2Cl_2) 9.9; 36.5; 120.8; 128.7; 130.5; 151.6; 153.9 (spectrum recorded after 36 hours).

3.3.9 Vacuum-line techniques

A vacuum-line was utilised in order to ensure that atmospheric moisture was excluded from the reactions. A mercury diffusion pump backed with a rotary oil pump enabled pressures of approximately 10^{-2} torr to be achieved. At this pressure the liquid reactants were readily distillable by the methods described below. All reactants were dried and degassed before use - the method is described below.

The vacuum-line is shown in Figure 1.

The ground glass joints on taps 3-6 enabled a variety of apparatus to be attached, ranging from standard round-bottomed flasks to the specially designed reaction flask (Figure 2), hanging burettes (Figure 3), and nmr tubes (Figure 4).

The following sections describe the basic techniques used in this work. The first two sections, (a) and (b), describe the techniques used to ensure anhydrous and low-pressure reaction conditions respectively. Section (c) describes the procedure for transfer of the reactants from either a hanging burette or flask, to the reaction flask, by distillation.

(a) Drying of solvents

The solvent was initially dried using conventional methods. The solvent was generally dichloromethane, dried over calcium hydride.

The solvent was placed in flask 1 together with calcium hydride. The flask and contents were then frozen with a liquid nitrogen bath and the apparatus was evacuated by opening taps 1, 2 and 7, initially with only the backing pump connected to the line. When a pressure of less than 1 mm Hg was achieved, tap 8 was closed and taps 9 and 10 were opened, and the system was pumped down to approx. 10^{-2} torr. After 15 minutes tap 1 was closed, as were taps 9 and 10, and tap 8 was opened. The contents of flask 1 were thawed and after 5 minutes were re-frozen and pumped down again. This freeze/pump/thaw process was repeated three times. Taps 1 and 2 were then closed, the vacuum-line being continuously pumped by the mercury diffusion pump. The solvent in flask 1 was refluxed for 2 hours by gently heating the flask and

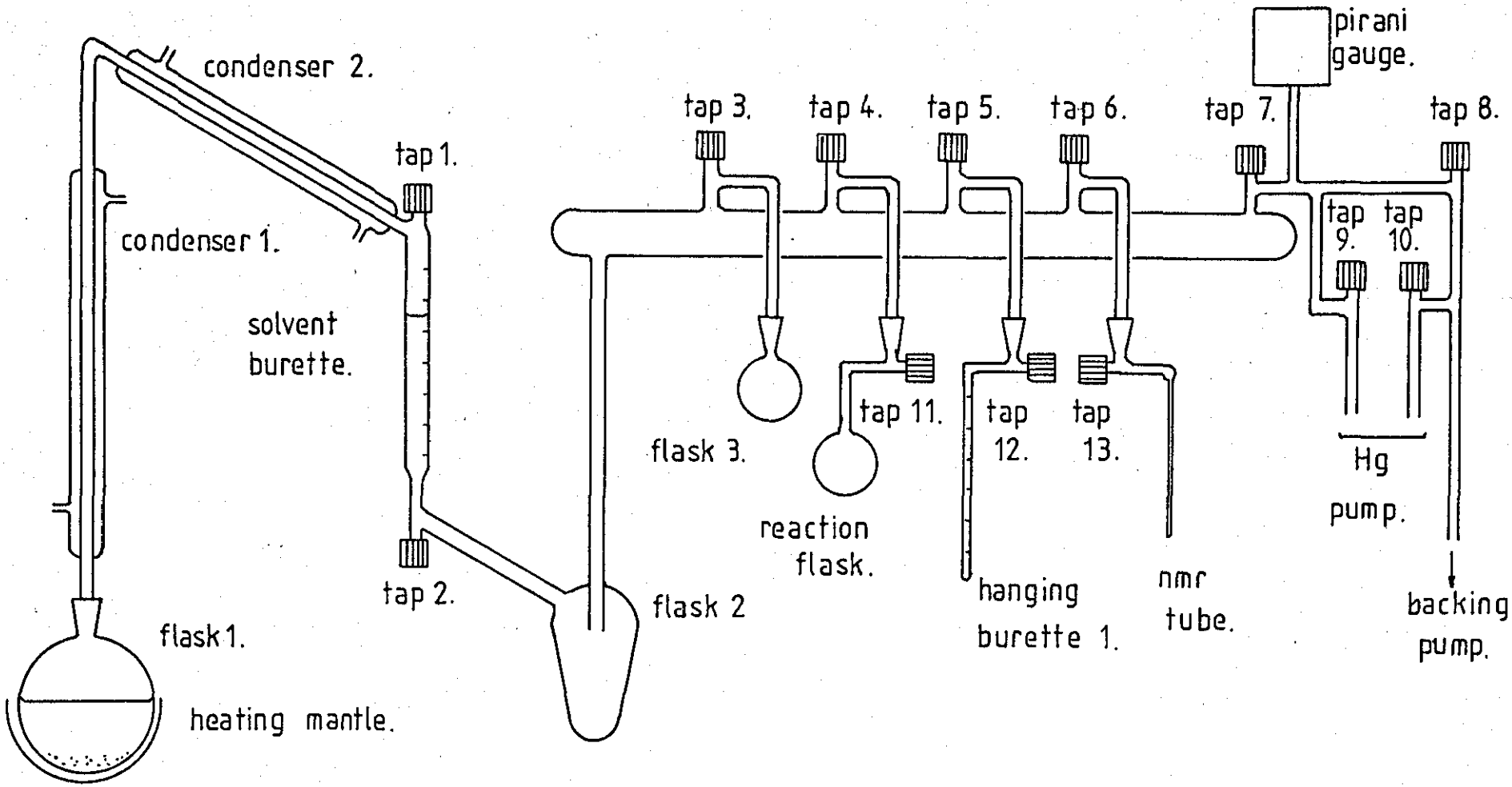


FIGURE 1.

VACUUM - LINE APPARATUS

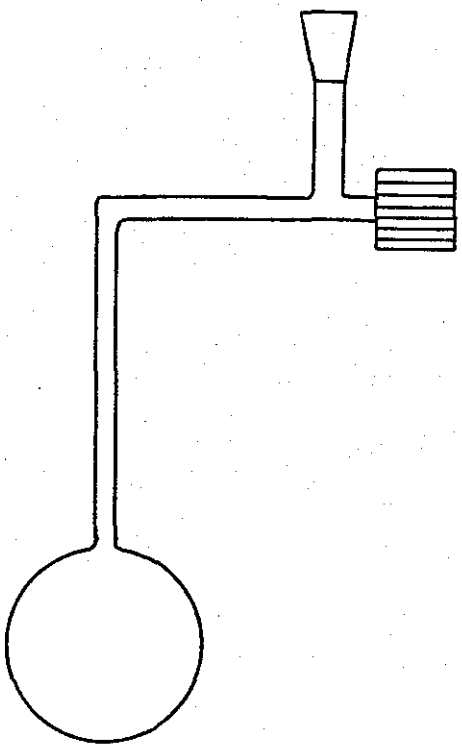


FIGURE 2

REACTION FLASK.

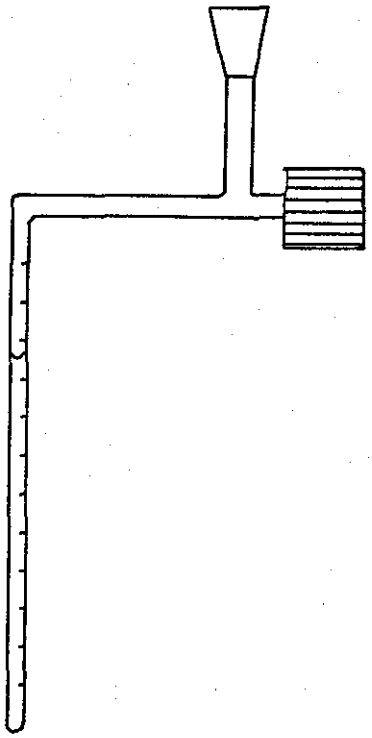


FIGURE 3

HANGING BURETTE

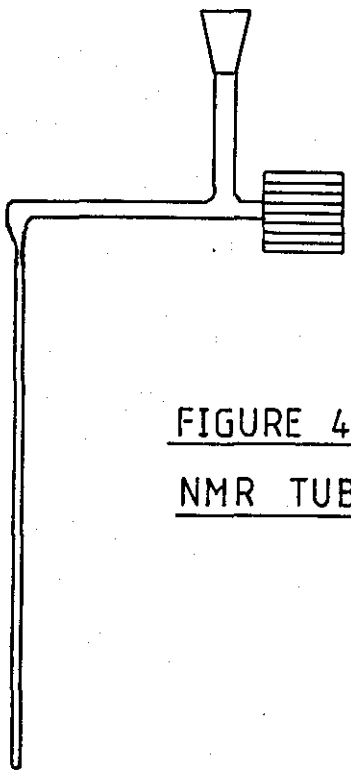


FIGURE 4

NMR TUBE

allowing cold water to circulate in condenser 1. The solvent was then distilled into the solvent burette by opening tap 1 and using condenser 2. Tap 1 was then closed and the heating mantle turned off. The dry solvent in the burette could then be run off as required into flask 2 to be distilled into the reaction flask.

Further dry solvents could be added by introducing them from flask 3, after having been through the freeze/pump/thaw process described above.

(b) Degassing of starting materials

This process was necessary to achieve the low pressures required for these experiments.

(i) Solids - All solids were pumped down using the mercury diffusion pump for at least 12 hours before use. Slight heating of the solid ensured that any water present was removed.

(ii) Liquids - The freeze/pump/thaw process described above ensured that all liquid reactants were degassed before being used in any experiment.

(c) Distillation of reactants

The four procedures described below were utilised in order to transfer reactants from one piece of apparatus to another.

(i) Transfer of solvent from solvent burette to reaction flask - The system was pumped down with taps 4, 7 and 11 open, and taps 2, 3, 5 and 6 closed. Tap 7 was then closed and the reaction flask was cooled with liquid nitrogen. Tap 2 was opened until the required amount of solvent had been run out, and was then closed. The reaction flask was kept at this temperature for 10 minutes, after which time tap 11 was closed, and tap 7 was opened. The solvent in the reaction flask was allowed to thaw. Addition of reactants to the reaction flask is described below.

(ii) Transfer of reactant from flask 3 to hanging burette - The reactant was purified and dried by conventional methods before being placed in flask 3. Itwas then frozen using liquid nitrogen and subjected to the freeze/pump/thaw procedure described above. With tap 3 closed, taps 5 and 12 were opened and pumped down as usual. Tap 7

was closed and the hanging burette 1 was cooled with liquid nitrogen. Tap 3 was opened until the hanging burette 1 appeared to be full, when it was closed. Tap 12 was then closed and the burette was allowed to come to room temperature. Tap 7 was opened and the system was pumped down once again.

(iii) Transfer of reactant from hanging burette to reaction flask - With taps 4 and 5 open and taps 11 and 12 closed the system was pumped down as usual. Tap 7 was then closed. The reaction flask was cooled with liquid nitrogen and taps 11 and 12 were opened until a measured amount of reactant had distilled into the cooled flask. Taps 11 and 12 were closed, tap 7 was opened, and the reaction flask was allowed to warm to the desired temperature. This procedure could be repeated for the addition of several reactants.

(iv) Transfer of reactant from flask 3 to reaction flask - A weighed amount of purified reactant was placed in flask 3, and was then subjected to the freeze/pump/thaw process described above. The reactant was distilled into the reaction flask using the same procedure as in (iii) above.

(v) Transfer of reactant from hanging burette to nmr tube - The procedure was generally as in (iii) above. Once all reactants had been distilled in, the tap 13 was closed, keeping the tube and contents in a liquid nitrogen bath. The tube was detached from the line and sealed using a gas/oxygen torch.

(d) Isolation of products

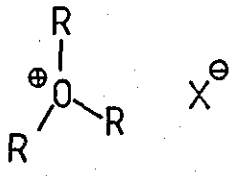
Once the reaction was complete, tap 11 was closed and the reaction flask was detached from the vacuum-line. Work-up was carried out in a dry-box under a dry nitrogen atmosphere. Full experimental details are given in the relevant experimental sections above.

CHAPTER 4

OXONIUM SALTS

4.1 Introduction

Meerwein first reported isolating trialkyloxonium salts (4) in 1937[167,7,130]. These were formed by the reaction between epichlorohydrin and boron trifluoride etherate in an excess of the appropriate ether.



R=alkyl.

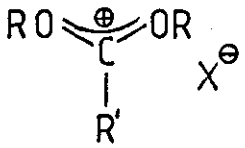
(4)

The yields of these salts decrease as the size of the alkyl group increases, and no oxonium salts have been prepared with alkyl groups larger than n-butyl.

These salts are stable only when an anion of low nucleophilicity such as BF_4^- is present. Salts have also been prepared with $SbCl_6^-$[143,144] SbF_6^-[130] and PF_6^-[145] as the counter-ion, the latter two being stable at room temperature, and also soluble in liquid sulphur dioxide and in methylene chloride.

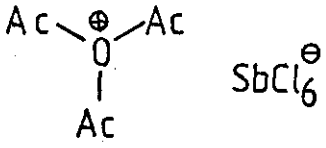
Because of the ease of elimination of positively charged alkyl groups, trialkyloxonium salts are strong alkylating agents. The synthesis and use of such salts is discussed in depth by Perst[80], Meerwein[191] and Baggett[102] and will not be covered further here.

Dialkoxycarbenium salts such as (111) are formed in the reaction of orthocarboxylic acid esters with BF_3 or $SbCl_5$[146].



(111)

R=alkyl.
R'=alkyl, H.
X=$SbCl_6$, BF_4.

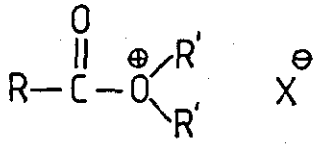


(112)

Such salts have been found to be strong alkylating agents. Indeed they are stronger alkylating agents than trialkyloxonium salts, which is shown by the fact that they readily alkylate ethers to trialkyloxonium salts whereas the reverse reaction (alkylation of carboxylic acid esters with trialkyloxonium salts) is impossible[147]. They are also capable of alkylating esters of higher carboxylic acids which are very weak nucleophiles. Further discussion of their preparation and reactions can be found in Perst[80].

Boekhoff[25] reported the isolation of triacetyloxonium hexafluoroantimonate (112) which is a pale yellow solid and is stable for several months at -70°C. This salt acts as an acylating agent and was investigated in connection with the cationic telomerisation of monomers like styrene or THF in the presence of acetic anhydride.

Acyldialkyloxonium salts (113) have been postulated as intermediates in many reactions (see section 4.2.1), and have been isolated on several occasions[16,17]. These salts are only stable at low temperatures (-20°C and below) and are known to decompose by O-alkyl and/or O-acyl

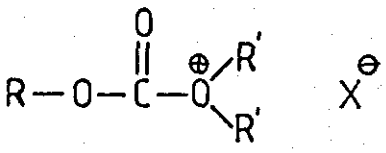


(113)

R'=alkyl.
X=$SbCl_6$,BF_4.

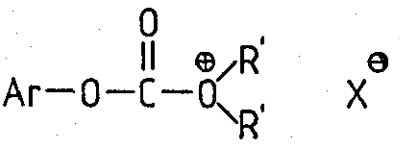
cleavage depending on the reaction conditions. Their preparation and mode of reaction are discussed fully in section 4.2.1.

There are no reports in the literature concerning the preparation or isolation of O-alkoxycarbonyl-O,O-dialkyloxonium (12) or O-phenoxycarbonyl-O,O-dialkyloxonium (114) salts. Formation of this latter group of salts by the alkylation of appropriate alkyl aryl carbonates has been investigated and the results are described in section 4.2.3. Preparation by routes similar to those described for the sulphonium salt analogues (see sections 3.2.2 and 3.2.3) has not been investigated. The salts of type (12) have not been investigated in this study.



(12)

R,R' = alkyl.
X = $SbCl_6$, BF_4.



(114)

Ar = Ph.
R' = alkyl.
X = $SbCl_6$, BF_4.

There appears to be no published work on the ^{13}C nmr spectra of salts of type (12), (113) and (114). Using ^{13}C nmr techniques it is possible to study this type of salt in order to ascertain where and how the charge is stabilised in the molecule. Our results are discussed in detail in the sections below.

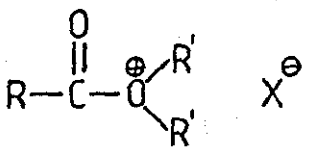
These salts appear to decompose readily in contact with moisture. Much of the early work was hindered greatly by this problem. Considerable time was spent developing techniques and apparatus which ensured anhydrous conditions. These are described more fully in the experimental section (section 4.3).

The sections that follow describe in detail the work carried out by the author in order to prepare and characterise salts of type (113) and (114).

4.2 Preparation and Reactions of α-Carbonyl Oxonium Salts

4.2.1 Reaction of acyl halides with ethers in the presence of a Lewis acid

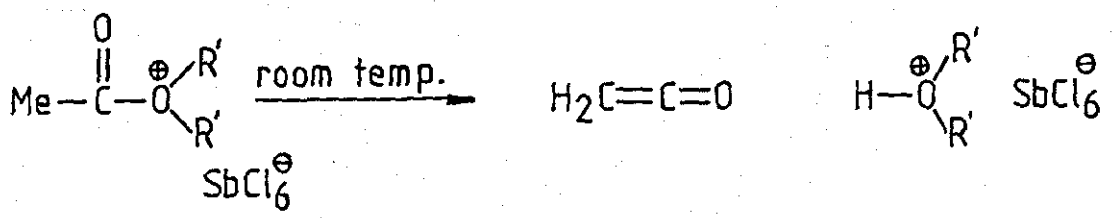
The cleavage of ethers using acyl halides or anhydrides in the presence of metal or non-metal halides has been well-documented[148,149]. These reactions lead to alkyl halides (from acyl halides) and carboxylic acid esters (or their adducts with the Lewis acid), presumably via an intermediate acyldialkyloxonium salt (113).



(113)

Meerwein[6] reported that a 1:1 diethyl ether/antimony pentachloride complex reacts with acetyl chloride at room temperature to give ethyl acetate and ethyl chloride. Acetic anhydride[149] gives ethyl acetate under similar reaction conditions. No intermediates of type (113) were isolated.

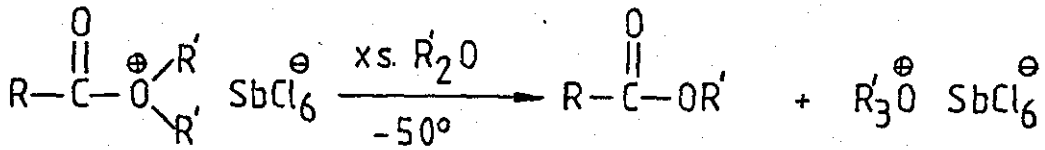
Klages[16] isolated several salts of type (113) by reaction of an acyl chloride (R = CH_3, C_2H_5) and antimony pentachloride with a dialkyl ether (R' = CH_3, C_2H_5). These salts are only stable at -20°C and below and are not well characterised. Thermal decomposition of the acetyldialkyloxonium salts gives not only the expected O-alkyl cleavage but also O-acyl cleavage. The dialkyl ether is seen as the dialkyloxonium salt (or its etherate), ketene being formed simultaneously.



O-Acetyltetrahydrofuranium tetrafluoroborate has been prepared by Meerwein by reaction of the tetrahydrofuran / boron trifluoride complex with acetyl fluoride, and is more stable than the acyclic hexachloro-

antimonates[17]. O-Alkyl cleavage of this salt (i.e. ring opening) using tetrahydrofuran initiates polymerisation of the latter.

This type of intermediate (113) has also been postulated in the preparation of trialkyloxonium salts from acyl halides and antimony pentachloride/ pentafluoride at low temperature in the presence of a ten molar excess of dimethyl ether or diethyl ether[130] i.e.



(113)

Low temperatures and an excess of the ether suppresses O-acyl cleavage and favours O-alkyl cleavage.

There appear to be no ^{13}C nmr data for O-acyldialkyloxonium salts in the literature. The ^{13}C nmr spectrum for triacetyloxonium hexafluoroantimonate has been reported by Boekhoff[25], and shows a carbonyl carbon at 196.3 ppm and a methyl carbon at 27.06 ppm (c.f. acetic anhydride: 175.4 ppm and 28.53 ppm respectively).

The section that follows describes our attempts to repeat the work of Klages in order to characterise the O-acyldialkyloxonium salts using ^1H nmr and ^{13}C nmr techniques. Also described are our attempts at preparing and isolating the O-benzoyldialkyloxonium salt equivalents of those prepared by Klages.

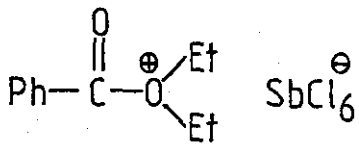
4.2.1.1 Reaction of benzoyl chloride with diethyl ether in the presence of antimony pentachloride

The reaction was studied using two sets of reaction conditions, one a preparative scale reaction, the other a reaction in an nmr tube.

When diethyl ether (1 equivalent) is added to a solution of antimony pentachloride (1 equivalent) in methylene chloride at -70°C, a cream-coloured solid is formed, which is presumably a 1:1 complex between diethyl ether and antimony pentachloride[150]. Addition of the benzoyl chloride (1 equivalent) gives no noticeable reaction at -70°C. On standing at -25°C for 7 days large yellow crystals are formed.

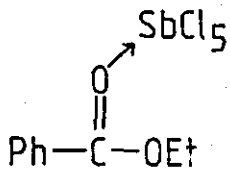
Filtration gives the crystals in 62% yield. No analysis was carried out on the filtrate.

Infrared analysis of the solid shows a carbonyl stretch peak at 1693 cm^{-1}. This is much lower than might be expected for the salt (115) and is attributed to a 1:1 complex between ethyl benzoate and



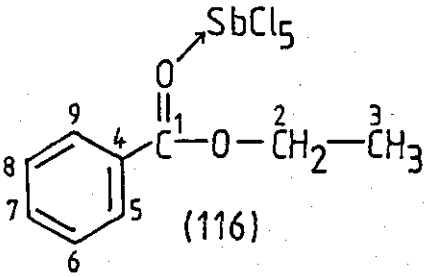
(115)

antimony pentachloride (116). This complex has been reported in the



(116)

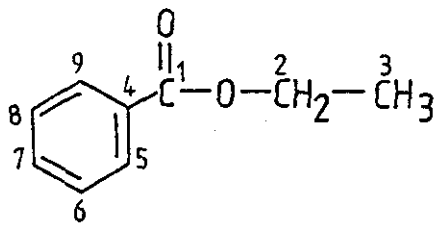
literature[151], and the nmr data also suggests its presence. ^1H Nmr analysis shows peaks at δ 1.87 (triplet, 3H, $-CH_3$), 5.32 (quartet, 2H, $-CH_2^-$), 7.55-8.05 (multiplet, 3H, aromatic) and 8.30-8.55 (multiplet, 2H, aromatic), which match well with a sample prepared by mixing equimolar amounts of ethyl benzoate and antimony pentachloride in d_2-methylene chloride at room temperature. The ^{13}C nmr shows peaks as follows:



(116)

1. 175.1 ppm	6. 129.5
2. 70.5	7. 137.6
3. 14.3	8. 129.5
4. 127.3	9. 133.2
5. 133.2	

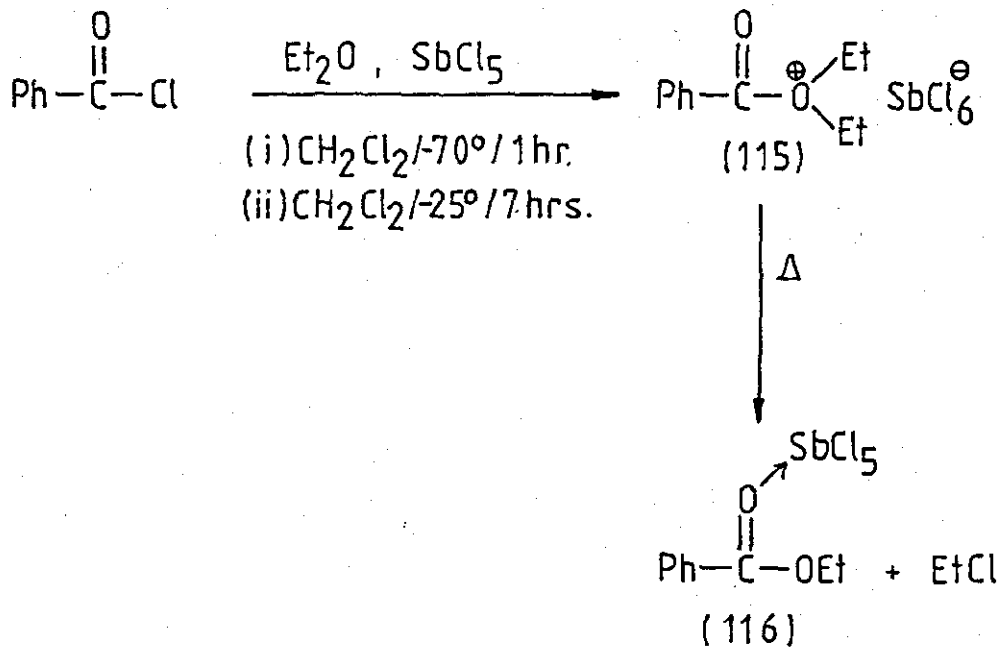
compare with:



1. 166.3 ppm	6. 128.4
2. 60.8	7. 132.8
3. 14.4	8. 128.4
4. 130.9	9. 129.7
5. 129.7	

ref: 140

This complex is formed by the route shown below, via the benzoyldiethyloxonium salt (115) which suffers nucleophilic attack by the hexachloroantimonate ion to give ethyl chloride and the complex (116). This O-alkyl cleavage is well known in the reaction of ethers with acyl halides catalysed by metal or non-metal halides[16,130,148], leading to alkyl halides and carboxylic acid esters or their adducts with Lewis acids. The thermal instability of the salts of type (115)

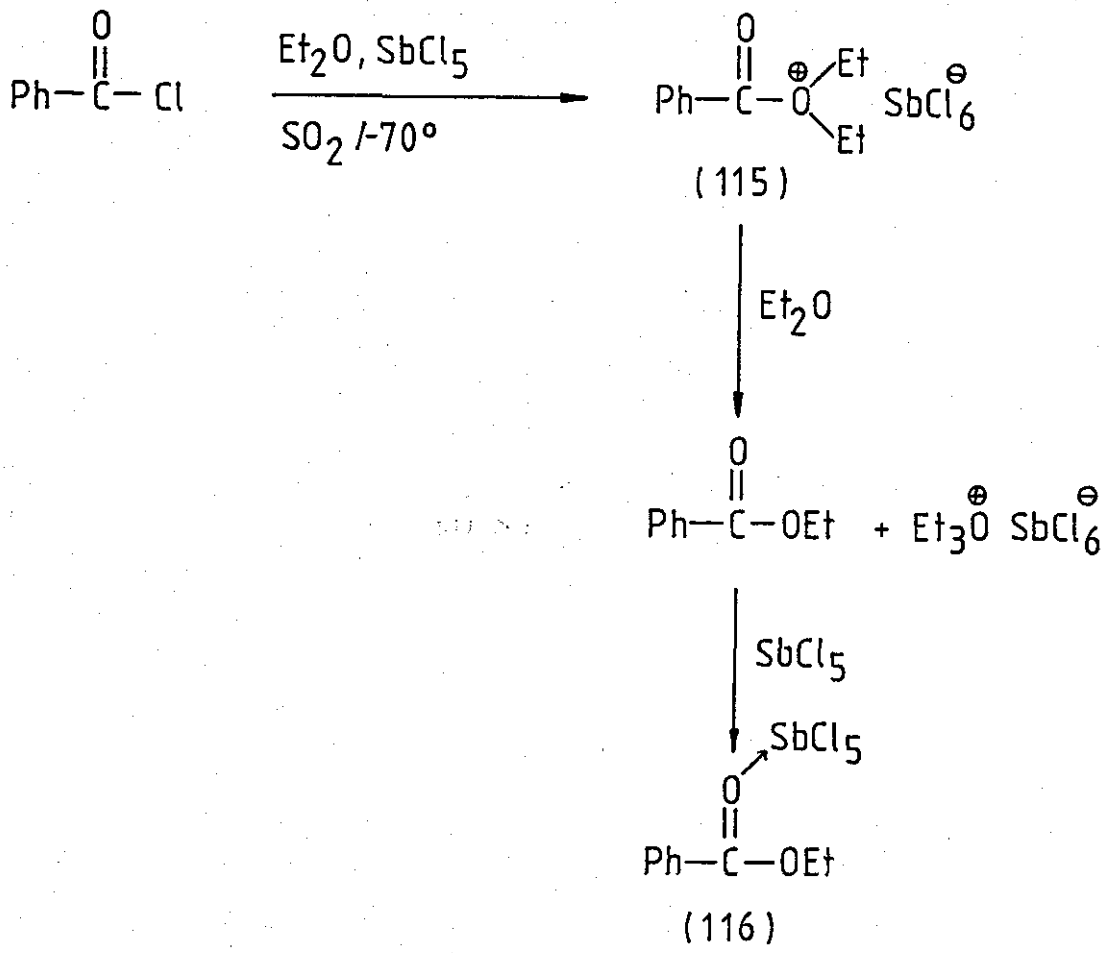


above is further illustrated in section 4.2.1.2 below.

In the nmr tube reaction, benzoyl chloride (1 equivalent) is added to a solution of antimony pentachloride (1 equivalent) in liquid sulphur dioxide at -70°C to give a cream-coloured solid that does not dissolve. This is the benzoyl chloride/antimony pentachloride complex. Addition of 1 equivalent of ether at -70°C gives a clear brown solution, which on standing overnight at -30°C turns red. ^{13}C Nmr analysis shows this to contain essentially the same products as our first reaction.

The major product is the ethyl benzoate/antimony pentachloride complex (116) (^{13}C nmr = 175.6; 137.1; 133.0; 129.6; other aromatic carbon not visible; 68.8; 13.2 ppm). There appears to be no unchanged benzoyl chloride present. The other aromatic carbon peaks are possibly

due to the presence of the benzoyl chloride/antimony pentachloride complex, although no definite assignments can be made. The peaks at 72.9 and 13.2 ppm are attributable to the diethyl ether/antimony pentachloride complex and are not unexpected in view of the reaction conditions. Triethyloxonium hexachloroantimonate can be seen in the ^{13}C nmr spectrum (83.8 and 12.9 ppm) which suggests that the scheme shown below is operational, i.e. the salt (115) is formed in the reaction but is decomposed by the free diethyl ether. The small peaks at 78.4, 41.1, 26.1 and 18.3 ppm are, as yet, unexplainable.



Both of these reactions show that whilst the salt (115) is formed in the reaction, it is too reactive to be isolated under these conditions. Further work is needed to optimise reaction conditions to ensure that dealkylation of the salt does not take place.

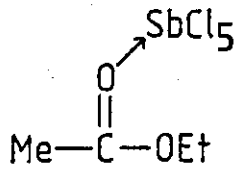
4.2.1.2 Reaction of acetyl chloride with diethyl ether in the presence of antimony pentachloride

This reaction was studied using a preparative-scale reaction, and a small-scale reaction in an nmr tube.

In the preparative-scale reaction a cream-coloured solid is formed when 1 equivalent of diethyl ether is added to a solution of antimony pentachloride (1 equivalent) in methylene chloride at -70°C. This is a 1:1 complex between diethyl ether and antimony pentachloride[150]. No immediate reaction is noticed when 1 equivalent of acetyl chloride is added to this solution at -70°C. After standing at -25°C for 22 hours, cooling to -70°C gives a yellow solid. Filtration gives a tacky, yellow solid in 37% yield. No analysis was carried out on the filtrate.

Analysis of the solid using 'H nmr and ^{13}C nmr techniques shows it to be a mixture of several products. Peaks at 72.0 and 13.4 ppm in the ^{13}C nmr spectrum suggest that the diethyl ether/antimony pentachloride complex is a major product. This is also supported by the 'H nmr spectrum which shows peaks at δ 1.53 (triplet) and δ 4.33 (quartet). This result is not surprising when one considers the reaction conditions, as diethyl ether is known to form complexes readily in the presence of antimony pentachloride[151].

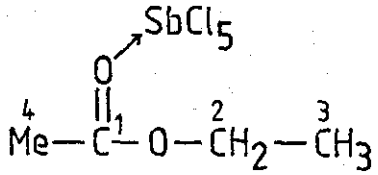
The ^{13}C nmr spectrum also suggests the presence of the 1:1 complex between ethyl acetate and antimony pentachloride (117) showing



(117)

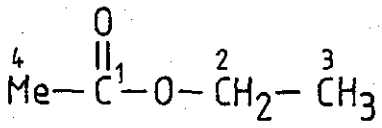
peaks at 21.4 and 182.8 ppm, the peaks for the ethyl carbons being at 72.0 and 13.4 ppm. We can compare these with the ^{13}C nmr spectrum of

ethyl acetate and find that similar changes have occurred to those seen in section 4.2.1.1 above. The proton nmr spectrum also supports



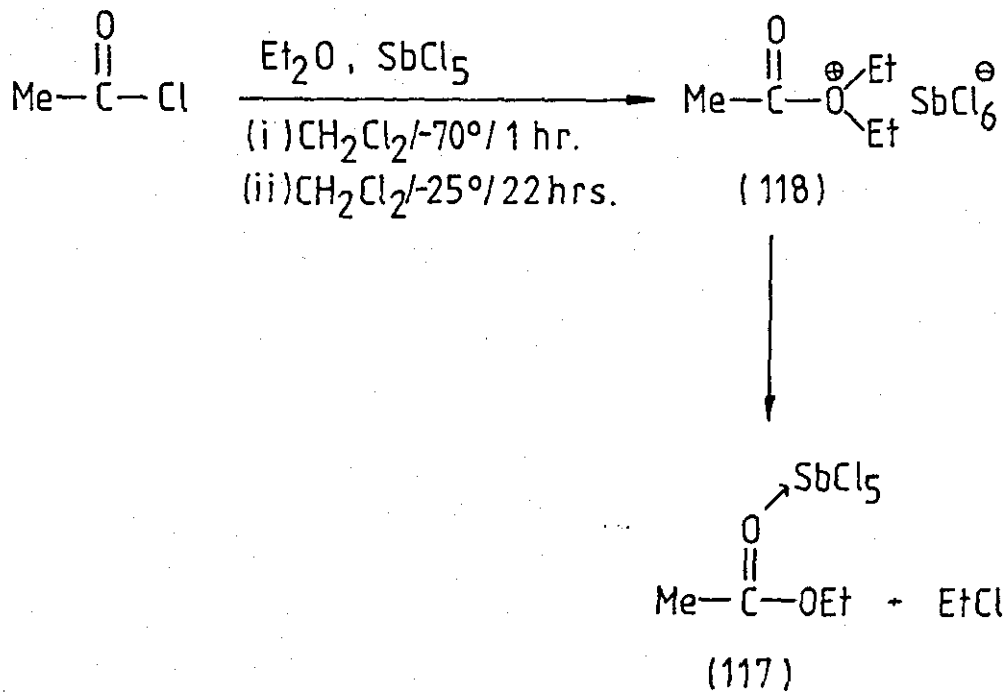
1. 182.8 ppm 3. 13.4
2. 72.0 4. 21.4

compare with:

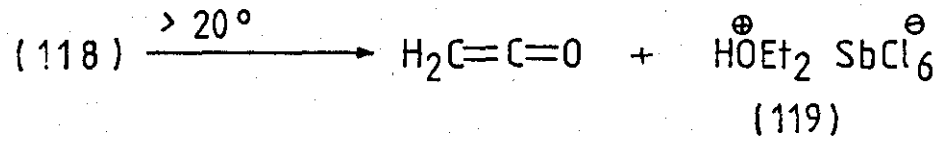


1. 171.6 ppm 3. 14.0
2. 61.0 4. 20.5 ref: 139

the presence of this complex, showing peaks at δ 1.53 (triplet), 4.33 (quartet) and 2.59 (singlet). This complex must be formed by the route shown below, via the acetyldiethyloxonium salt (118). Reaction of (118) with hexachloroantimonate ion gives ethyl chloride and the complex (117).



The salt (118) is also known to decompose at temperatures greater than -20°C[16] to give ketene and the protonated ether (119). There is no evidence for the presence of (119) or ketene (^{13}C nmr (lit.[152] = 196.4; 3.86 ppm) in the product.



(118) $\xrightarrow{> 20°}$ $H_2C{=}C{=}O$ + $\overset{\oplus}{H}OEt_2\ \overset{\ominus}{SbCl_6}$ (119)

The peaks at δ 3.08 (small singlet), 3.18 (small singlet) and 4.62 (small quartet) in the ^1H nmr spectrum and 3.0 ppm (small singlet) in the ^{13}C nmr spectrum cannot be explained as yet, but seem to be very minor products.

These results indicate that although the salt (118) is formed in this reaction, it is too reactive to be isolated using our experimental procedures. We found it impossible to repeat the work of Klages[16] who supposedly isolated this salt in 66% yield. It is possible that formation of the acetylium ion followed by a controlled addition of diethyl ether at low temperature might yield the salt in reasonable yield, but lack of time halted any further investigation of the reaction.

4.2.2 Reaction of carboxylic acid esters with alkylating agents

The weakly nucleophilic nature of the carbonyl oxygen in a carboxylic acid ester makes alkylation difficult even in the presence of strong alkylating agents.

Although the alkylation of acyclic esters has been found to occur only with very strong alkylating agents, alkylation of cyclic esters occurs more readily. Meerwein[138] reported that both γ-butyraldehyde and phthalide are readily alkylated by triethyloxonium tetrafluoroborate to give the expected O-alkylated products. Both 5- and 6-membered ring lactones have been found to give the expected O-alkylated products when treated with methyl fluorosulphate[75]. These apparent anomalies are possibly explained by comparing the conformation of the reacting groups in the acyclic ester with that of the cyclic molecule. Esters are known to adopt a conformation with the C- and O-alkyl groups transoid to minimise dipolar repulsion. In the cyclic ester this cannot

occur and it is thus destabilised relative to the acyclic molecule.

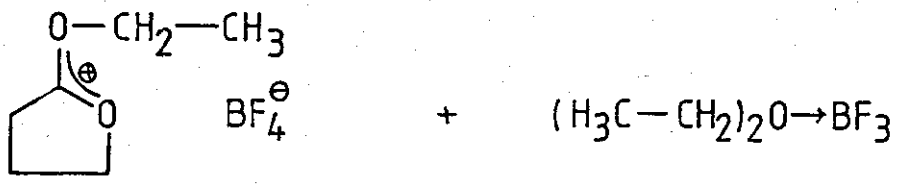
Acyclic esters remain unchanged when treated with trialkyloxonium salts[147]. Alkylation of higher carboxylic esters has been achieved in good yield using dialkoxycarbenium salts[105]. Ethyl acetate undergoes methyl-ethyl exchange with methyl fluorosulphate, whereas methyl acetate remains unchanged under the same conditions[74]. The expected O-alkylated product is presumably an intermediate but is not observed. Dialkylhalonium ions[106] have been found to be highly reactive alkylating agents, and readily alkylate esters[153,154].

The following sections describe our work in this area and our attempts at recording the ^{13}C nmr spectra of the alkylated products formed in the reactions.

4.2.2.1 Alkylation of γ-butyrolactone

Ethylation using triethyloxonium tetrafluoroborate gave the results shown in table 7. The ^{13}C nmr spectrum shows that the reaction has gone to completion after 3 days at room temperature.

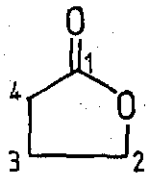
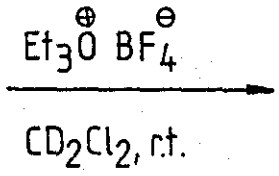
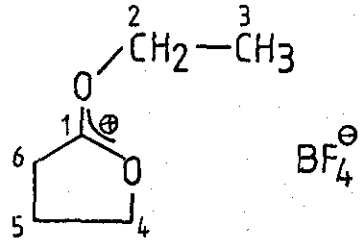
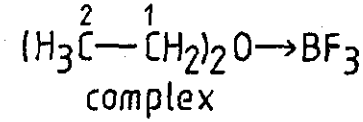
The ^{13}C nmr spectrum shows that alkylation has taken place solely



on the carbonyl oxygen, as expected[138,155].

The carbonyl carbon has moved from 178.1 ppm in the lactone to 196.4 ppm, a downfield shift of 18.1 ppm. This is consistent with the stabilisation of the positive charge as shown above, and compares well with the change in chemical shift seen when N,N-dialkylamides are O-alkylated (see section 2.2.8). In this latter case the positive charge is accommodated more on nitrogen atom and thus the change in chemical shift is smaller than in this example above, where it is more evenly spread. The chemical shifts of the methylene and methyl carbons

Table 7

Ester	Conditions	Products
1. 		 

1. 178.1 ppm
2. 68.8
3. 22.3
4. 27.8

1. 196.4 ppm
2. 77.3
3. 13.2
4. 85.0
5. 20.9
6. 32.0

1. 67.1 ppm (broad)
2. 14.6 (broad)

of the added alkyl group also reflect this stabilisation of charge. They show peaks at 77.3 and 13.2 ppm respectively compared with 84.4 and 12.2 ppm for the equivalent carbons in triethyloxonium tetrafluoroborate where the positive charge is solely on one oxygen atom.

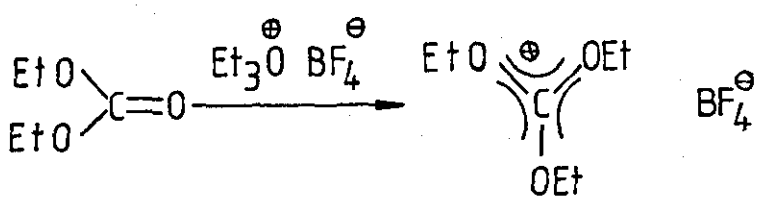
The chemical shifts of the carbon atoms in the ring system have also changed in the alkylated product. As expected, the methylene carbon next to the oxygen in the ring has moved downfield considerably (16.2 ppm) which again reflects the stabilisation of the positive charge in the molecule. The methylene carbon adjacent to the carbenium carbon has also moved downfield but by a much smaller amount (4.2 ppm). The remaining methylene carbon has in fact moved upfield by 1.4 ppm, which is similar to the situation seen when the shift of the methyl carbons in triethyloxonium salts is compared with that of the methyl carbon in diethyl ether itself.

Peaks are also seen at 67.1 and 14.6 ppm which are attributable to the diethyl ether/boron trifluoride complex. This is partially due to the decomposition of triethyloxonium tetrafluoroborate in solution, but the peaks are broadened due to the exchange reaction that takes place with the diethyl ether liberated during the reaction.

4.2.3 Reaction of carbonic acid esters with alkylating agents

There are few examples of this type of reaction in the literature.

The reaction of triethyloxonium tetrafluoroborate with diethyl carbonate has been reported by Meerwein[138,146]. The triethoxycarbonium salt (120) is a crystalline solid and is formed in 45% yield.



(120)

This result contrasts with the findings of Alder who reported that dimethyl carbonate is not alkylated by methyl fluorosulphate[75].

Our experiments were carried out in order to clarify the situation. ^{13}C Nmr spectroscopy was utilised as the products would be expected to have considerably different spectra to the starting materials. There appear to be no literature reports of the ^{13}C nmr spectra of trialkoxycarbonium ions.

4.2.3.1 Alkylation of methyl phenyl carbonate

Methylation using trimethyloxonium tetrafluoroborate gave the results shown in table 8. The ^{13}C nmr spectrum shows that no reaction has taken place under these reaction conditions.

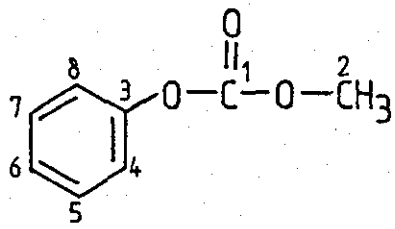
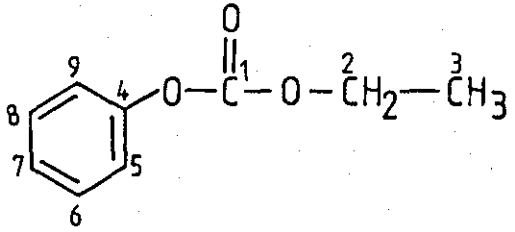
This is not unexpected as carbonates have been found to be inert to strong alkylating agents such as methyl fluorosulphate[75]. It is possible however, that dialkylhalonium salts[106] could provide us with an alkylating agent capable of alkylating carbonates, but unfortunately no further work could be carried out on this reaction.

4.2.3.2 Alkylation of ethyl phenyl carbonate

Ethylation using triethyloxonium tetrafluoroborate gave the results shown in table 8. The ^{13}C nmr spectrum shows that no reaction has taken place under these conditions, other than the formation of the diethyl ether/boron trifluoride complex from the decomposition of triethyloxonium tetrafluoroborate in solution.

Again this was not unexpected, but unfortunately the reaction could not be investigated further using more reactive alkylating agents due to lack of time.

Table 8

Carbonate	Conditions	Products
1. 	$Me_3\overset{\oplus}{O}\ \overset{\ominus}{BF_4}$ / CD_2Cl_2/SO_2, -20°	unchanged starting materials.
2. 	$Et_3\overset{\oplus}{O}\ \overset{\ominus}{BF_4}$ / CD_2Cl_2, r.t.	as above + $(H_3\overset{2}{C}-\overset{1}{C}H_2)_2O\rightarrow BF_3$

1. 154.3 ppm
2. 55.2
3. 151.4
4. 121.1
5. 129.5
6. 127.0
7. 129.5
8. 121.1

1. 154.2 ppm
2. 65.2
3. 14.4
4. 151.9
5. 121.7
6. 129.9
7. 126.4
8. 129.9
9. 121.7

1. 70.5 ppm
2. 13.3

4.3 Experimental

The general experimental details as laid out in section 2.3 apply.

Solvents and reagents were purified and dried by conventional methods[85]. All reactions were carried out under as near anhydrous conditions as possible. The vacuum-line system is described fully in Chapter 3.

The yields are based on the total mass of starting materials used in the reaction, unless otherwise stated i.e. 75% = 75% of material recovered as product(s).

Where possible the identity of the product was verified by comparison of the spectral details with those of an authentic sample.

The results are discussed in detail in sections 4.2.1 to 4.2.3 above.

4.3.1 Reaction of acyl halides with ethers in the presence of a Lewis acid

4.3.1.1 Reaction of benzoyl chloride with diethyl ether in the presence of antimony pentachloride

This reaction was studied using two different procedures, one a preparative scale reaction, the other being carried out in an nmr tube. Details are given below.

(a) Preparative scale reaction - The apparatus is described in section 2.3.2. Antimony pentachloride (0.04 mole) in methylene chloride (25 cm^3) was cooled to -70°C, and to this was added diethyl ether (0.04 mole) which gave a cream-coloured solid after several minutes. After leaving this to stand for 30 minutes at -70°C, benzoyl chloride (0.04 mole) was added. The reaction was left to stand for 7 days at approx. -25°C. On standing at this temperature the solution became dark brown, and large yellow crystals formed on the bottom of the flask. The solvent was filtered off, and the solid was washed twice with methylene chloride (2 x 10 cm^3) at -70°C. The crystals were filtered off and dried under vacuum at room temperature to give large, yellow crystals in 62% yield, m.pt. 98-100°C.

IR (C=O) Nujol, 1693 cm^{-1}.
'H nmr δ (CD_2Cl_2) 1.87 (t, 3H, $-CH_3$); 5.32 (q, 2H, $-CH_2-$); 7.55-8.05 (m, 3H, aromatic); 8.30-8.55 (m, 2H, aromatic).
^{13}C nmr ppm (CD_2Cl_2) 14.3; 70.5; 127.3; 129.5; 133.2; 137.6; 175.1.

(b) Nmr tube reaction - The nmr tube was equipped with a rubber septum to ensure additions were carried out under anhydrous conditions. To a solution of antimony pentachloride (0.36 mmole) in liquid sulphur dioxide (0.3 cm^3) at -70°C, was added benzoyl chloride (0.35 mmole) which gave an immediate cream-coloured solid that would not dissolve. After 1 hour at this temperature, diethyl ether (0.35 mmole) was added at -70°C, and on shaking all the solid went into solution to give a clear, brown solution. After standing at approx. -30°C overnight, a deep-red, clear solution was formed. CD_2Cl_2 (0.2 cm^3) was added for locking the ^{13}C nmr spectrometer.

No 'H nmr spectrum run.
^{13}C nmr ppm (SO_2/CD_2) at -20°C 12.9; 13.2; 18.3; 26.1; 41.1; 68.8 (broad); 72.9 (broad); 78.4; 83.4; 129.6; 130.9; 133.0; 137.1; 139.2; 175.6.

4.3.1.2 Reaction of acetyl chloride with diethyl ether in the presence of antimony pentachloride

This reaction was studied using a preparative scale reaction.

(a) Preparative scale reaction - The apparatus is described in section 2.3.2. To a solution of antimony pentachloride (3.9 mmole) in methylene chloride (2.5 cm^3) at -70°C was added diethyl ether (3.9 mmole) to give an immediate cream precipitate which did not dissolve at -70°C. Acetyl chloride (3.9 mmole) was then added, which had no immediate effect. The mixture was allowed to come slowly to -25°C over a period of 6 hours, and left at this temperature for a further 16 hours. The reaction was then cooled to -70°C when a yellow solid came down. This was filtered off, washed with dichloromethane (2 x 1 cm^3) at -70°C to give a yellow/brown solid which was dried under vacuum for 8 hours at -40°C to -30°C. Yield = 37%. No melting point could be taken as the sample readily liquefied at room temperature. The sample was taken up

in d_2-methylene chloride (0.5 cm^3).

^1H nmr δ (SO_2/CD_2Cl_2) at -20°C 1.53 (5); 2.59 (s); 3.08 (s); 3.18 (s); 4.33 (q); 4.62 (q).

^{13}C nmr ppm (SO_2/CD_2Cl_2) at -20°C 3.0; 13.4; 21.4; 72.0; 182.8.

4.3.2 Reaction of carboxylic acid esters with alkylating agents

The alkylating agent was prepared according to a standard procedure (see section 2.3.7). The alkylation was carried out under anhydrous conditions using one of the procedures given in section 2.3.7.

(a) Preparation of carboxylic acid esters

γ-Butyrolactone as supplied by Aldrich Chemical Co. Ltd. was used without further purification.

^{13}C nmr ppm ($CDCl_3$) 22.3; 27.8; 68.8; 178.1 (lit.[40]).

(b) Alkylation of carboxylic acid esters

The ^{13}C nmr spectral data given below relate only to the alkylated product. Those due to excess starting material or other by-products such as ether, etc., are not shown but are mentioned in the discussion of these reactions.

4.3.2.1 γ-Butyrolactone

Ethylated using method C to give a clear solution after 3 days. Reaction went to completion.

^{13}C nmr ppm (CD_2Cl_2) 13.2; 20.9; 32.0; 77.3; 85.0; 196.4 (spectrum recorded after 3 days).

4.3.3 Reaction of carbonic acid esters with alkylating agents

The carbonic acid esters were prepared according to the procedure below (section a). The alkylating agents were prepared according to standard procedures (section 2.3.8).

The alkylations were carried out under anhydrous conditions using one of the procedures given in section 2.3.8.

(a) Preparation of carbonic acid esters

Methyl phenyl carbonate

Methanol (0.3 mole) was added dropwise and with stirring to a cooled solution of phenyl chloroformate (0.2 mole) and pyridine (0.2 mole) in diethyl ether (200 cm^3). The pyridine hydrochloride was filtered off, the solution was washed with water (2 x 150 cm^3) and then dried over anhydrous $MgSO_4$. Filtration, and evaporation of the solvent under reduced pressure, gave the crude product. Distillation gave the pure carbonate in 73% yield, b.pt. 194-195°C (lit.[157] 190-200°C).

IR (C=O) 1760 cm^{-1}.

^1H nmr δ ($CDCl_3$) 3.75 (s, 3H); 7.09 (m, 5H).

^{13}C nmr ppm ($CDCl_3$) 55.2; 151.4; 121.1; 129.5; 127.0; 154.3.

Ethyl phenyl carbonate

Prepared according to the procedure above in 82% yield, b.pt. 228-229°C (lit.[158] 227.5-229.5°C).

IR (C=O) 1760 cm^{-1}.

^1H nmr δ ($CDCl_3$) 1.31 (t, 3H); 4.22 (q, 2H); 7.16 (m, 5H).

^{13}C nmr ppm ($CDCl_3$) 14.4; 65.2; 151.9; 121.7; 129.9; 126.4; 154.2.

(b) Alkylation of carbonic acid esters

The ^{13}C nmr spectral data given below relate only to the alkylated product. Those due to excess starting material or other by-products such as ether, etc., are not shown but are mentioned in the discussion of these reactions.

4.3.3.1 Methyl phenyl carbonate

Methylated using method A to give an opaque solution after 3 days. Spectrum run after 3 days at -25°C.

^{13}C nmr ppm (CD_2Cl_2/SO_2) -20°C O-Alkylation product not seen (see discussion).

4.3.3.2 Ethyl phenyl carbonate

Ethylated using method C to give a clear solution after 12 hours.

Spectra run after 12 hours and 2 weeks.

^{13}C nmr ppm (CD_2Cl_2) O-Alkylation product not seen (see discussion).

REFERENCES

1. A.T. Bottini, Sel. Org. Transform., 1970, 1, 89.
2. A. von Oefele, Liebigs Ann. Chem., 1864, 132, 82.
3. "The Chemistry of the Sulphonium Group", ed. C.J.M. Stirling and S. Patai, Wiley, 1981.
4. C.J.M. Stirling, in "Organic Chemistry of Sulphur", ed. S. Oae, Plenum Press, New York, 1977, p.473.
5. G.C. Barrett, in "Comprehensive Organic Chemistry", ed. D.H.R. Barton and W.D. Ollis, 1979, 3, 105.
6. H. Meerwein, E. Battenberg, H. Gold, E. Pfeil, G. Willfang, J. Prakt. Chem., 1939, 154, 83-156; Chem. Abstr., 1940, 34, 2325(s).
7. H. Meerwein, G. Hinz, P. Hofmann, E. Kroning, E. Pfeil, J. Prakt. Chem., 1937, 147, 257.
8. H. Perst, Oxonium Ions in Organic Chemistry, Academic Press, London and New York, 1971.
9. H. Meerwein, in Houben-Weyl, "Methoden der Organischen Chemie", Vol. 6, Part 3, Georg Thieme Verlag, Stuttgart, 1965, p.325.
10. N. Baggett, in "Comprehensive Organic Chemistry", ed. D.H.R. Barton and W.D. Ollis, 1979, 1, 813.
11. R.G. Pearson, Chem. Brit., 1967, 3, 103; J. Am. Chem. Soc., 1963, 85, 3533; J. Am. Chem. Soc., 1967, 89, 1827.
12. F.R. Jones, P.H. Plesch, J. Chem. Soc., Dalton Trans., 1979, 927.
13. J.V. Paukstelis, M. Kim, J. Org. Chem., 1974, 39 (11), 1503.
14. F. Klages, E. Zange, Liebigs Ann. Chem., 1957, 607, 35.
15. M.G. Ahmed, R.W. Alder, G.H. James, M.L. Sinnott, M.C. Whiting, J. Chem. Soc., Chem. Commun., 1968, 1533.
16. F. Klages, E. Mühlbauer, G. Lukasczyk, Chem. Ber., 1961, 94, 1464.
17. H. Meerwein, D. Delfs, H. Morschel, Angew. Chem., 1960, 72, 927.
18. H. Minato, T. Miura, M. Kobayashi, Chem. Lett., 1977, 609.
19. J.V. Paukstelis, M. Kim, J. Org. Chem., 1974, 39 (11), 1499.
20. M.G. Ahmed, R.W. Alder, J. Chem. Soc., Chem. Commun., 1969, 1389.
21. G.L. Nelson, G.C. Levy, J.D. Cargioli, J. Am. Chem. Soc., 1972, 94, 3089.
22. G.A. Olah, A.M. White, Ibid., 1969, 91, 5801.
23. G.A. Olah, P.W. Westerman, D.A. Forsyth, Ibid., 1975, 97, 3419.
24. G.A. Olah, A.M. White, Ibid., 1967, 89, 7072.

25. H. Boekhoff, W. Heitz, Makromol. Chem., 1979, 180, 1055.
26. J.D. Hobson, J.G. McCluskey, J. Chem. Soc. C, 1967, 2015.
27. J.A. Campbell, J. Org. Chem., 1957, 22, 1259.
28. M. Matzner, R.P. Kurkjy, R.J. Cotter, Chem. Rev., 1964, 64, 645.
29. T. Hopkins, J. Chem. Soc., 1920, 117, 278.
30. W. Gerrard, F. Schild, Chem. Ind. (London), 1954, 1232.
31. M.G. Reinecke, R.G. Daubert, J. Org. Chem., 1973, 38 (19), 3281.
32. G. Just, G. Paul Donnini, Can. J. Chem., 1977, 55, 2998.
33. G. Kraiss, K. Nádor, Tetrahedron Lett., 1971, 57.
34. T.A. Montzka, J.D. Matiskella, R.A. Partyka, Ibid., 1974, 1325.
35. R.A. Olofson, Y.S. Yamamoto, D.J. Wancowicz, Ibid., 1977, 1563.
36. R.A. Olofson, R.C. Schnur, L. Bunes, J.P. Pepe, Ibid., 1977, 1567.
37. K.C. Rice, J. Org. Chem., 1975, 40 (12), 1850.
38. M.M. Abdel-Monem, P.S. Portoghese, J. Med. Chem., 1972, 15, 208.
39. G.R. Krow, J. Reilly, J. Am. Chem. Soc., 1975, 97, 3837.
40. E.H. Flynn, H.W. Murphy, R.E. McMahon, Ibid., 1955, 77, 3104.
41. J.W. Bastable, J.D. Hobson, W.D. Riddell, J. Chem. Soc., Perkin Trans., 1972, 2205.
42. F.E. Ziegler, G.B. Bennett, J. Am. Chem. Soc., 1973, 95, 7458.
43. A.S. Bailey, A.G. Holton, J.F. Seager, J. Chem. Soc., Perkin Trans., 1972, 1003.
44. H.A. Hageman, Org. React., 1953, 7, 198.
45. G. Olofsson, Acta Chem. Scand., 1967, 21, 1114.
46. J.L. Douglas, J. Meunier, Can. J. Chem., 1975, 53, 3681.
47. F.E. Ziegler, G.B. Bennett, Tetrahedron Lett., 1970, 29, 2545.
48. P. Beak, R.J. Trancik, D.A. Simpson, J. Am. Chem. Soc., 1969, 91, 5073.
49. G.A. Olah, P. Schilling, J.M. Bollinger, J. Nishimura, Ibid., 1974, 96, 2221.
50. W. Bremser, Carbon-13 NMR Spectral Data, Verlag Chemie, Weinheim, 1981, CNMR 6218.
51. W. Bremser, Ibid., CNMR 4507.
52. H. Adkins, Q.E. Thompson, J. Am. Chem. Soc., 1949, 71, 2242.
53. W.M. Dehn, A.A. Ball, Ibid., 1914, 36, 2091.
54. R.C. Paul, D. Singh, S.S. Sandhu, J. Chem. Soc., 1959, 315.
55. L.W. Jones, H.F. Whalen, J. Am. Chem. Soc., 1925, 47, 1343.

56. G. Entenmann, Synthesis, 1975, 377.
57. G. Entenmann, Tetrahedron, 1976, 31, 3131.
58. R.J. Boatman, H.W. Whitlock, J. Org. Chem., 1976, 41 (18), 3050.
59. J.A. Settepani, G.R. Pettit, Ibid., 1970, 35 (3), 843.
60. J.Y. Nedelec, J. Sorba, D. Lefort, Synthesis, 1976, 821.
61. D.P.N. Satchell and R.S. Satchell in "The Chemistry of Acyl Halides", ed. S. Patai, Interscience, New York, 1972, Chapter 4.
62. E. Wedekind, Liebigs Ann. Chem., 1901, 318, 99.
63. D. Cook, Can. J. Chem., 1967, 40, 2362.
64. G.A. Olah, S.J. Kuhn, W.S. Tolgyesi, E.B. Baker, J. Am. Chem. Soc., 1962, 84, 2733.
65. H. Meerwein, H. Maier-Hüser, J. prakt. Chem., 1932, 134, 51.
66. L.W. Jones, H.F. Whalen, J. Am. Chem. Soc., 1925, 47, 1343.
67. F. Seel, Z. Anorg. Allg. Chem., 1943, 250, 331.
68. B.C. Challis and J.A. Challis, in "The Chemistry of Amides", ed. Jacob Zabicky, Interscience, John Wiley, 1970, Chapter 13.
69. M. Matsui, Mem. Coll. Sci. Eng. Kyoto, 1909, 2, 37; Chem. Abstr. 1910, 98 (1), 695.
70. J.W. Janus, J. Chem. Soc., 1955, 3551.
71. R.E. Benson, T.L. Cairns, Org. Synth., volume 31, p.72.
72. S. Peterson, E. Tietze, Liebigs Ann. Chem., 1959, 623, 166.
73. H. Meerwein, W. Florian, N. Schön, G. Stopp, Ibid., 1961, 641, 1.
74. M.G. Ahmed, R.W. Alder, G.H. James. M.L. Sinnott, M.C. Whiting, J. Chem. Soc., Chem. Commun., 1968, 1533.
75. R.W. Alder, Chem. Ind. (London), 1973, 983.
76. R. Roger, D.G. Neilson, Chem. Rev., 1961, 61, 179.
77. R.F. Borch, Tetrahedron Lett., 1968, (1), 61.
78. L. Weintraub, S.R. Oles, N. Kalish, J. Org. Chem., 1968, 33 (4), 1679.
79. H. Muxfeldt, W. Rogalski, J. Am. Chem. Soc., 1965, 87, 933.
80. Loughborough University of Technology, ^{13}C nmr spectrum no. 190.
81. W. Bremser, reference 50, CNMR 6162.
82. Loughborough University of Technology, ^{13}C nmr spectrum no. 524.
83. D.J. Hart, W.T. Ford, J. Org. Chem., 1974, 39, 363.
84. Loughborough University of Technology, ^{13}C nmr spectrum no. 452.
85. A.I. Vogel, "A Textbook of Practical Organic Chemistry", 4th edit., Longman, London and New York, 1978.

86. S.H. Pine, B.L. Sanchez, J. Org. Chem., 1971, 36 (6), 829.
87. Beilstein, Handbuch der Organischen Chemie, 20, 276.
88. H.A. Bruson, C.W. MacMullen, J. Am. Chem. Soc., 1941, 63, 270.
89. J. Décombe, C.R. Acad. Sci., 1933, 196, 866.
90. C.J. Pouchert, "The Aldrich Library of Infrared Spectra", 3rd edit., Aldrich Chemical Company, Milwaukee, 1981, 3, spectrum 1050A.
91. W. Bremser, reference 50, CNMR 7997.
92. W. Bremser, reference 50, CNMR 6201.
93. A.P.N. Franchimont, Recl. Trav. Chim. Pay-Bas, 2, 332, 342.
94. F. Hallmann, Ber. Dtsch. Chem. Ges., 1876, 9, 846.
95. O. Wallach, Liebigs Ann. Chem., 214, 193.
96. J. von Braun, Ber. Dtsch. Chem. Ges., 36, 2287.
97. H. Meerwein, Org. Synth., coll. vol. 5, 1096.
98. H. Meerwein, Ibid., 1080.
99. A.P.N. Franchimont, F. Klobbie, Recl. Trav. Chim. Pays-Bas, 8, 299.
100. M. Barker, L. Hunter, N.G. Reynolds, J. Chem. Soc., 1948, 874.
101. G.A. Olah, M. Calin, J. Am. Chem. Soc., 1968, 90, 401.
102. F.E. Ray, J.L. Farmer, J. Org. Chem., 1943, 8, 391.
103. C.G. Swain, E.R. Thornton, J. Am. Chem. Soc., 1961, 83, 4033.
104. A.J. Boulton, A.C. Gripper Gray, A.R. Katritzky, J. Chem. Soc. B, 1967, 911.
105. S. Kabuß, Angew. Chem. Int. Ed. Engl., 1966, 5 (7), 675.
106. G.A. Olah, J.R. DeMember, Y.K. Mo, J.J. Svoboda, P. Schilling, J.A. Olah, J. Am. Chem. Soc., 1974, 96, 884.
107. T. Mukaiyama, K. Hagio, H. Takei, K. Saigo, Bull. Chem. Soc. Jpn., 1971, 44, 161.
108. V. Franzen, H.J. Schmidt, C. Mertz, Chem. Ber., 1961, 94, 2942.
109. T. Hashimoto, K. Ohkubo, H. Kitano, K. Fukui, Nippon Kagaku Zasshi, 1966, 87, 456; Chem. Abstr., 1966, 65, 15259g.
110. R.W. LaRochelle, B.M. Trost, L. Krepski, J. Org. Chem., 1971, 36, 1126.
111. E.J. Corey, M. Jautelat, W. Oppolzer, Tetrahedron Lett., 1967, 2325.
112. G.B. Butler, B.M. Benjamin, J. Am. Chem. Soc., 1952, 74, 1846.
113. C.C.J. Culvenor, W. Davies, N.S. Heath, J. Chem. Soc., 1949, 282.
114. H. Böhme, G. Lerche, Chem. Ber., 1967, 100, 2125.
115. E.L. Gustus, P.G. Stevens, J. Am. Chem. Soc., 1933, 55, 378.
116. T. Oishi, M. Mori, Y. Ban, Chem. Pharm. Bull., 1971, 19 (9), 1863.
117. M. Mori, M. Shiozaura, Y. Ban, T. Oishi, Ibid., 1971, 19 (10), 2033.
118. G. Barbarella, Org. Magn. Resonance, 1976, 8, 108.

119. Loughborough University of Technology, ^{13}C nmr spectrum no. 288.
120. H. Meerwein, K. Zenner, R. Gipp, Liebigs Ann. Chem., 1965, 688, 67.
121. F. Klages, A. Gleissner, R. Ruhnau, Chem. Ber., 1959, 92, 1834.
122. F. Knoll, M-F. Müller-Kalben, R. Appel, Ibid., 1971, 104, 3716.
123. W. Bremser, reference 50, CNMR 11174.
124. W. Bremser, reference 50, CNMR 0503.
125. P. Beak, Acc. Chem. Res., 1976, 9, 230.
126. D.N. Kevill, in "The Chemistry of Acyl Halides", ed. S. Patai, Interscience, New York, 1972, chapter 12.
127. D.N. Kevill, W.A. Reis, J.B. Kevill, Tetrahedron Lett., 1972, 957.
128. C.J. Pouchert, "The Aldrich Library of Infrared Spectra", Aldrich Chemical Co., Milwaukee, 1970, spectrum 157C.
129. W. Bremser, reference 50, CNMR 2975.
130. R. Szymanski, H. Wieczorek, P. Kubisa, S. Penczek, J. Chem. Soc., Chem. Commun., 1976 (2), 33.
131. W. Bremser, reference 50, CNMR 633.
132. C.J. Pouchert, reference 128, spectrum 779A.
133. C.J. Pouchert, reference 128, spectrum 759C.
134. C.J. Pouchert, reference 128, spectrum 711G.
135. G.A. Olah, P.W. Westerman, J. Am. Chem. Soc., 1973, 95, 3706.
136. T. Oishi, M. Mori, Y. Ban, Tetrahedron Lett., 1971 (21), 1777.
137. T. Oishi, M. Mori, Y. Ban, Chem. Pharm. Bull., 1971, 19 (9), 1871.
138. H. Meerwein, P. Borner, O. Fuchs, H.J. Sasse, H. Schrodt, J. Spille, Chem. Ber., 1956, 89, 2060.
139. G.A. Olah, P.W. Westerman, J. Org. Chem., 1973, 38, 1986.
140. W. Bremser, reference 50, CNMR 5618.
141. R.B. Baker, E. Emmet Reid, J. Am. Chem. Soc., 1929, 51, 1567.
142. L.S. Pratt, E. Emmet Reid, Ibid., 1915, 37, 1934.
143. F. Klages, H. Meuresch, Chem. Ber., 1952, 85, 863.
144. F. Klages, H. Meuresch, Ibid., 1953, 86, 1322.
145. G.A. Olah, J.A. Olah, J.J. Svoboda, Synthesis, 1973, 490.
146. H. Meerwein, Angew. Chem., 1955, 67, 374.
147. H. Perst, reference 8, pp. 70-72.
148. R.L. Burwell Jnr., Chem. Rev., 1954, 54, 637.
149. H. Meerwein, H. Maier-Hüser, J. Prakt. Chem., 1932, 134, 51.
150. W. Carlton-Williams, J. Chem. Soc., 1876, 30, 463.

151. A. Rosenheim, W. Stellmann, Ber. Dtsch. Chem. Ges., 1901, 34, 3380.
152. G.A. Olah, J.M. Denis, P.W. Westerman, J. Org. Chem., 1974, 39, 1206.
153. G.A. Olah, J.R. DeMember, J. Am. Chem. Soc., 1969, 91, 2113.
154. G.A. Olah, J.R. DeMember, J. Am. Chem. Soc., 1970, 92, 718, 2562.
155. M.K. Kaloustian, F. Khouri, Tetrahedron Lett. 1981, 22 413.
156. Bruker ^{13}C Data Bank, volume 1, spectrum 364.
157. P. Cazeneure, C.R. Acad. Sci., 127, 112.
158. A. Peratoner, Gazz. Chim. Ital., 28 (1), 236.