A STUDY OF THE CHEMISTRY
OF THIETAN-3-ONES AND RELATED SUBSTANCES

by

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A thesis submitted for the Degree
of Doctor of Philosophy of the
University of Aston in Birmingham
1982

THE UNIVERSITY OF ASTON IN BIRMINGHAM

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SUMMARY

The chemistry of some novel derivatives of Thietan-3-ones has been studied. These thietanones have been prepared by the treatment of certain ketones with thionyl chloride in the presence or absence of pyridine. The stereochemistry of the thietanones was studied using nuclear magnetic resonance spectroscopy. The intermediates found during the formation of the thietanones have been shown to be the β-ketosulfinyl chlorides or the β-ketosulfenyl chloride depending on the nature of the ketone.

A certain new compounds, dithiolanone and thiolanone were synthesized by the treatment of dibromoketones with sodium sulfide and by the treatment of the β-ketosulfinyl chlorides with thionyl chloride respectively. Cyclization of the β-ketosulfenyl chlorides and β-ketosulfinyl chlorides was attempted using pyridine or triethylamine.

The nucleophilic reactions of the chlorothietanones have been studied using pyrrolidine, morpholine, piperidine, methanol, benzylmercaptan and hydrazine derivatives.

The hydrazine derivatives have been shown to attack both the C-2 and C-3 carbon of the thietanone. The other nucleophiles used only attack the C-2. When water is used as the nucleophile, carbon-sulfur cleavage occurs. It was found that the case of the nucleophilic reactions of the chlorothietanone may be correlated with the basicities and the sp^2 character of carbon -2. The reduction of the 2-chlorothietanone was investigated using different reducing reagents.

Treatment of the thietanone with sulfuryl chloride was shown not only to chlorinate the former but also to cleave the carbon-sulfur bond of the thietanone.

Treatment of the benzylidenethietanone with thionyl chloride did not give a dichloro-adduct as previously reported. In fact the product was found to be α- chloro-β-chloro α-chlorosulfenyl thietanone.

The mechanism of the reactions has been studied and discussed using both chemical and spectroscopic evidence.

Key words:

Thietan-3-ones, Nucleophilic reactions, Thionyl chloride, Ketones.

STATEMENT

I, S. Pourabbas, declare that this thesis has not been carried out in collaboration with others. Neither has it been submitted for any other award.

I would like to dedicate this Thesis to
my mother, brother and also in memory of
my father

ACKNOWLEDGEMENTS

I wish to express my sincere thanks to my supervisor, Mr J S Pizey, for his constant advice, encouragement, guidance and continual unfailing interest throughout the course of this work.

Also, I would like to thank Dr A Gaines and Mrs J Gaines for their help in enabling me to finish the course.

I am also indebted to the following laboratory staff for the instrumental analysis, Mrs V M Clenton for infrared spectra, Mr M C Perry for mass spectra, Mr E J Hartland for NMR spectra and Miss C Jakeman for elemental analysis.

Finally, I would like to thank Mrs J Coulthard and Mrs J Domone for typing this thesis.

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INTRODUCTION

CHAPTER ONE

INTRODUCTION

1 - a: The reactions of thionyl chloride with acids, alcohols, ketones and unsaturated compounds.

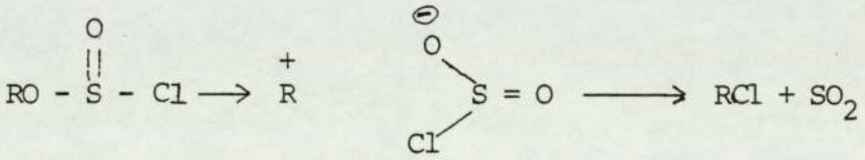
The reactions of thionyl chloride with organic compounds have long been recognised and large numbers have been reported in the literature. The most important reaction of thionyl chloride is the replacement of a hydroxyl group by chlorine in alcohols and carboxylic acids.

$$R - OH + SOCl_2 \longrightarrow RCl + SO_2 + HCl$$

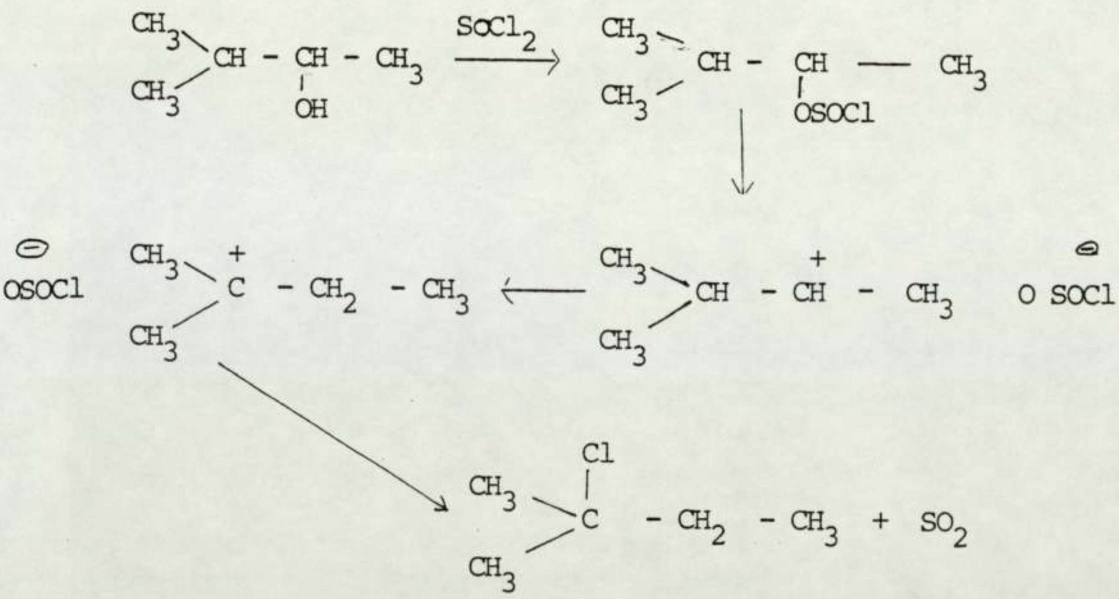
The replacement of hydroxyl groups may occur by three different paths. It may proceed with retention of configuration by a chlorine atom entering the site previously occupied by the hydroxyl group. Replacement may occur with partial or complete inversion of configuration or molecular rearrangement may take place. Bartletts group (1) has shown that the reaction proceeds via a sulfite intermediate, which affords chlorosulfinate when attacked by chloride ions.

$$2ROH + SOCl_2 \xrightarrow{-\ HCl} (RO)_2SO \xrightarrow[SOCl_2]{} 2ROSOCl$$

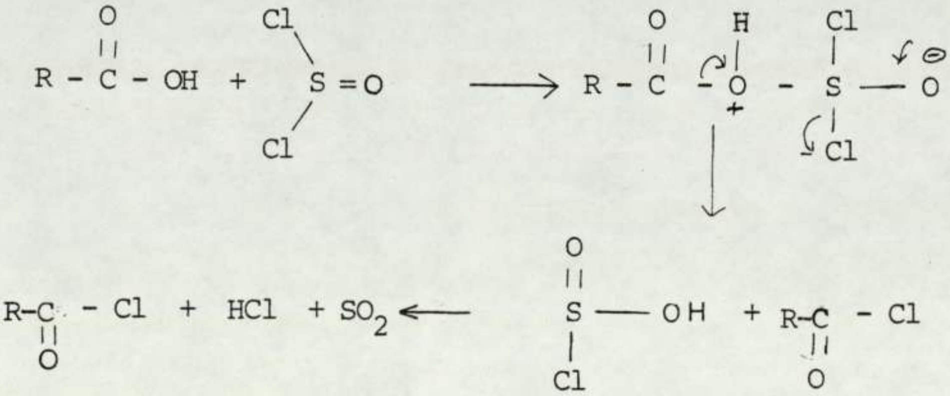
In the absence of added base the chlorosulfinate slowly dissociates into an ion pair and the halogen attacks the carbocation formed by a SNi mechanism (2).



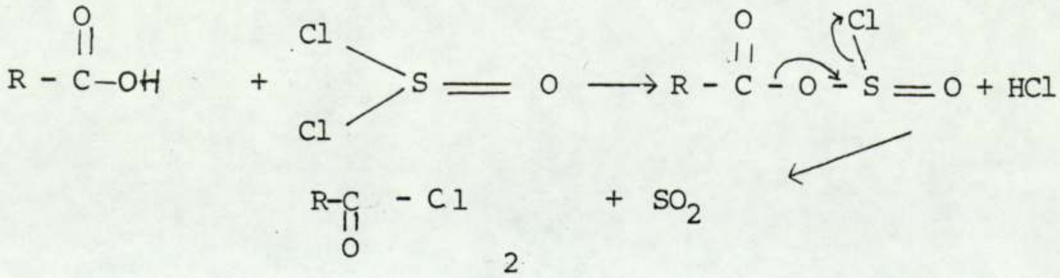
However, the intermediate carbocation itself rearranges to give the tertiary chloride (3).



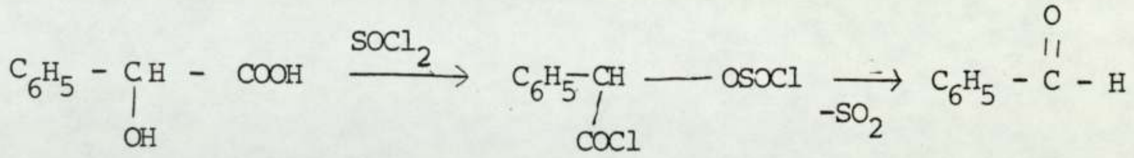
Aliphatic and aromatic carboxylic acids react with thionyl chloride in an analogous way to alcohols. The reactions of carboxylic acids with thionyl chloride have been studied by Beg and Singh(4, 5). They suggested the rate of the reaction increases with an increase in the dielectric constant of the medium, the reactivity of the acid decreases with increased electronegativity of groups adjacent to the acylprotons, and the reactivity of the acid decreases even more with increased steric bulk of the acid.



Gerrard and Thrush(6) have suggested another reaction pathway.

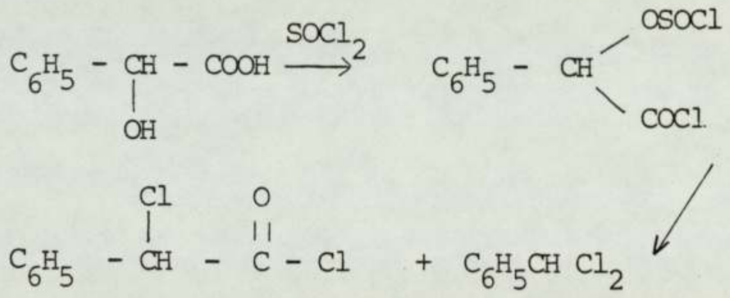


Mandelic acid afforded the chlorosulfite as an intermediate, which then decomposed to benzaldehyde$^{(7)}$.



$$C_6H_5-\underset{OH}{\underset{|}{C}H}-COOH \xrightarrow{SOCl_2} C_6H_5-\underset{COCl}{CH}-OSOCl \xrightarrow[-SO_2]{} C_6H_5-\overset{O}{\overset{\|}{C}}-H$$

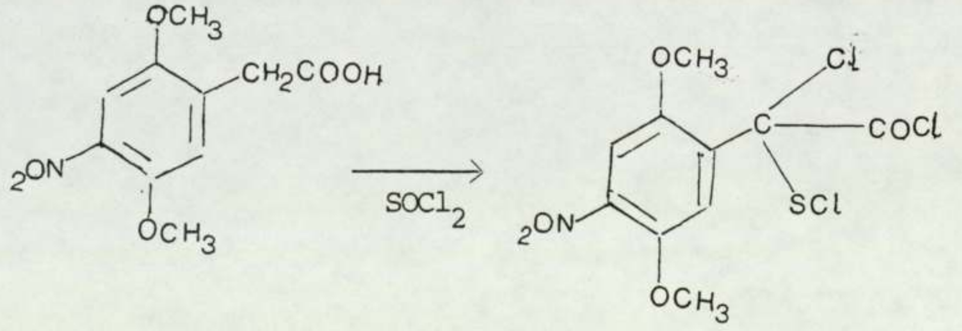
Carre and Libermann$^{(8)}$ showed the formation of α-chloro-α-phenylacetic acid chloride and benzylidene dichloride when mandelic acid was treated with thionyl chloride.

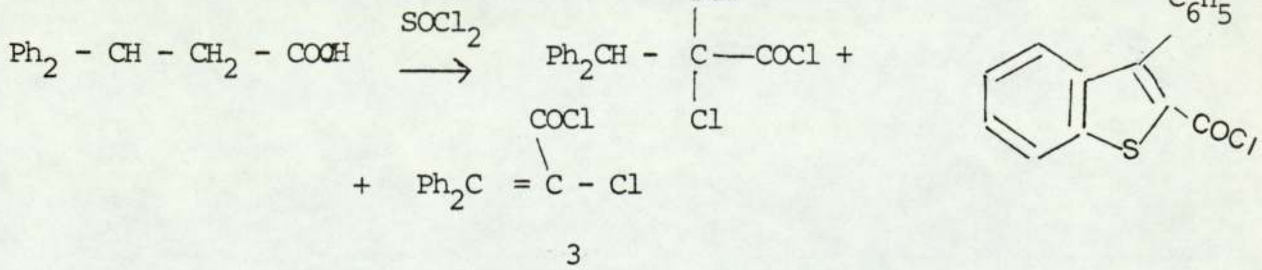


$$C_6H_5-\underset{OH}{\underset{|}{C}H}-COOH \xrightarrow{SOCl_2} C_6H_5-CH\begin{matrix}OSOCl\\COCl\end{matrix}$$

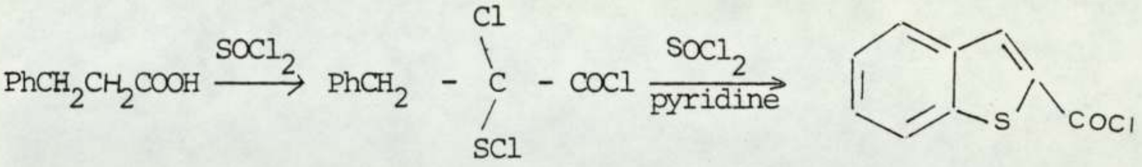
$$\longrightarrow C_6H_5-\overset{Cl}{\overset{|}{C}H}-\overset{O}{\overset{\|}{C}}-Cl + C_6H_5CH\,Cl_2$$

Simon et al.$^{(9)}$, Oka and Hara$^{(10)}$ have reported a reaction in which carboxylic acid containing activated protons in the α-position to the carbonyl group give a α-chloro-α-sulfenyl chloride on treatment with thionyl chloride.





The carboxylic acid 1 with thionyl chloride gave a benzo(b)thiophene 2 (11,12)

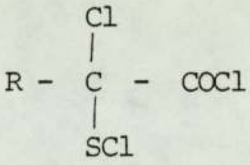


1 2

The reaction of the monosubstituted acetic acid 3 with thionyl chloride in the presence of a tertiary amine produced the α-chloro-α-sulfenyl chloride 4 (13-15). The ketone 5 with thionyl chloride also gave an α-chloro-α-sulfenyl chloride 6.

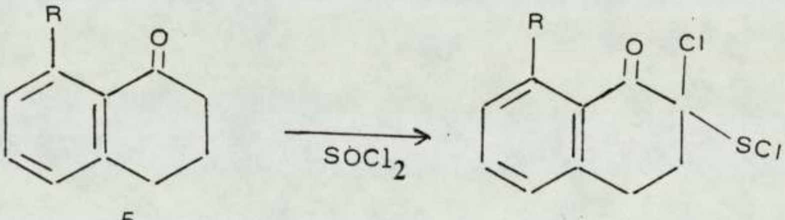
$R-CH_2-CO_2H$

3



$R-C(Cl)(SCl)-COCl$

4



5 6

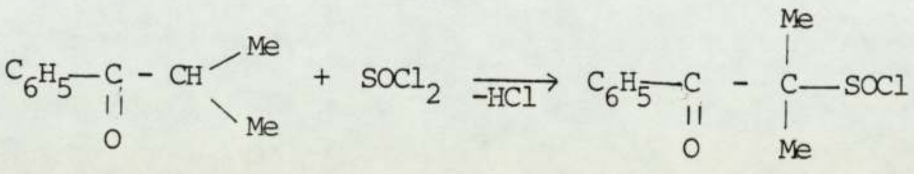
The reaction between thionyl chloride and ketones gives a variety of products depending both on the structure of the ketone and on the reaction conditions. Pizey and Symeonides (16) formulated two basic rules explaining the reactions.

I : The reactivity of α-protons followed the sequence tertiary > secondary >primary.

II : The extent of reactivity of α-protons towards thionyl chloride: α-protons of aliphatic acyclic ketones react with thionyl chloride provided two alpha tertiary groups are not formed as a result of the reaction, rule 2 does not apply to ketones containing a phenyl group in the alpha-position i.e. aryl ketones.

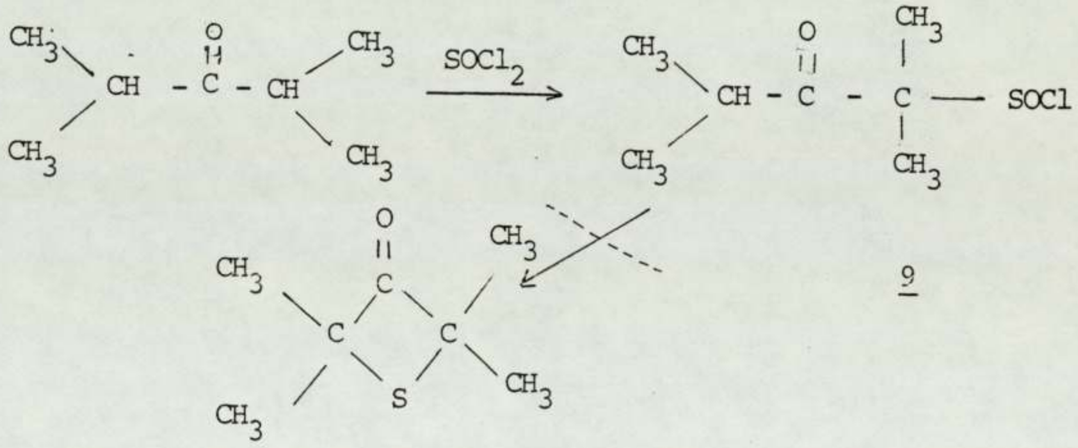
The ketones are classified according to the number of α, α′ protons present in the molecule.

A : The presence of one proton in the α-position in a ketone 7 produces the α-sulfinyl chloride 8 (16).



7 8

B : The presence of two protons, one α and one α′, in a ketone gives a sulfinyl chloride e.g. di-isopropyl ketone with thionyl chloride gave the sulfinyl chloride 9



10

but di-isopropyl ketone on treatment with thionyl chloride even in the presence of pyridine and on heating did not give the tetramethylthietan-3-one 10.

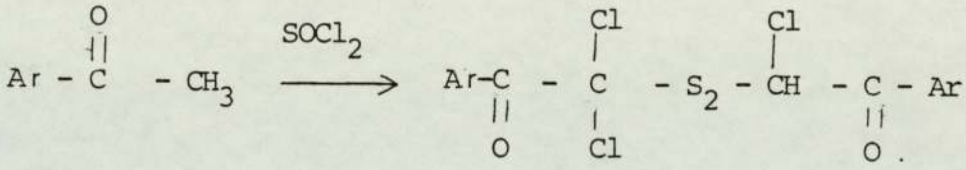
C : The presence of two protons in the-α-position in a ketone has not been investigated, but it has been anticipated that the α-chloro-α-chlorosulfenyl would form, similarly to carboxylic acids containing the α-methylene group.

D : The presence of three protons in the α-position in a ketone gives a variety of products. Acetophenone has been reported to give an α-keto-acid chloride 11 on treatment with thionyl chloride at 50 - 60° (17).

$$C_6H_5 - CO - CH_3 \xrightarrow{SOCl_2} C_6H_5 - CO{-}COCl$$

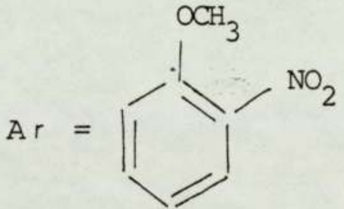
11

The reaction of acetophenone derivatives with thionyl chloride has been studied by Pizey and Symeonides (18) and Voss and Gunther (19). Voss and Gunther (19) have proposed the structure of 12.



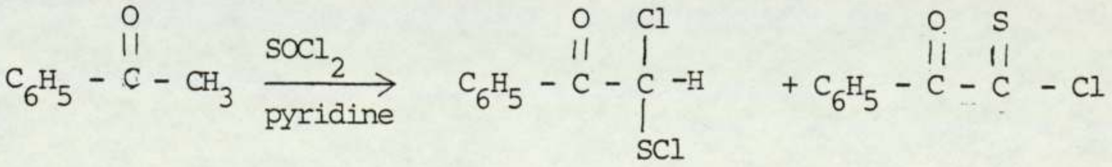
$$Ar - \overset{O}{\overset{\|}{C}} - CH_3 \xrightarrow{SOCl_2} Ar{-}\underset{\underset{O}{\|}}{C} - \overset{Cl}{\overset{|}{\underset{\underset{Cl}{|}}{C}}} - S_2 - \overset{Cl}{\overset{|}{CH}} - \underset{\underset{O}{\|}}{C} - Ar .$$

12



Oka and Hara (20) studied the reaction of acetophenone with thionyl chloride. Thus acetophenone with thionyl chloride in the presence of pyridine gave a mixture of 13 and 14.

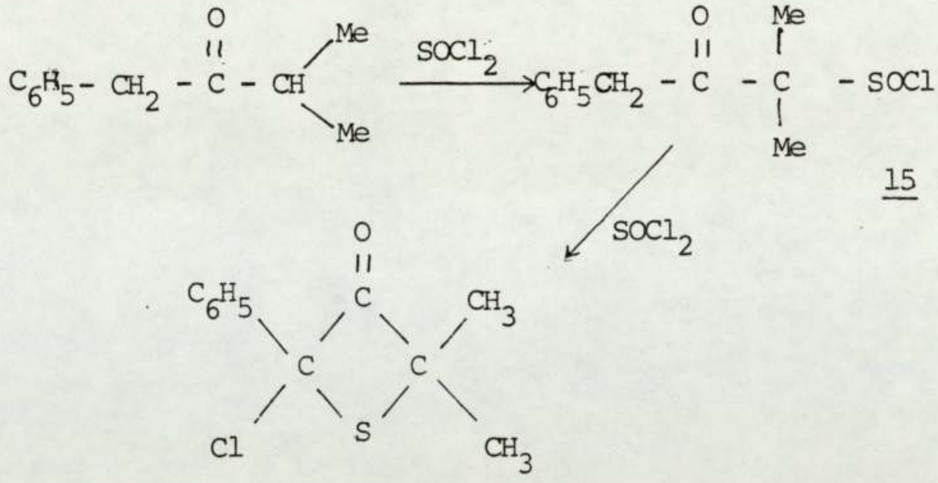
The α-chloro-α-sulfenyl chloride 13 can be easily dehydrochlorinated to thioacyl chlorides 14.



$$C_6H_5 - \overset{O}{\overset{\|}{C}} - CH_3 \xrightarrow[\text{pyridine}]{SOCl_2} C_6H_5 - \overset{O}{\overset{\|}{C}} - \overset{Cl}{\overset{|}{\underset{\underset{SCl}{|}}{C}}} -H \quad + C_6H_5 - \overset{O}{\overset{\|}{C}} - \overset{S}{\overset{\|}{C}} - Cl$$

13 14

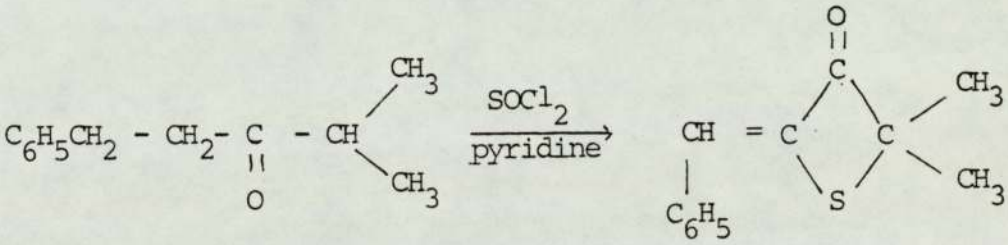
E : The presence of three protons, two α and one α′, e.g.benzyl isopropyl ketone produces a thietanone 16.



15

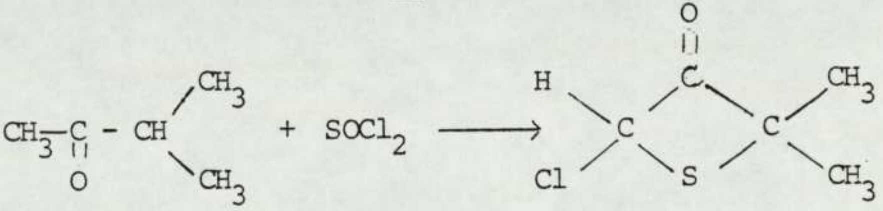
16

The intermediate of this reaction is a sulfinyl chloride 15 which then cyclizes to the chlorothietanone 16. 2-Methyl-5-phenylpentan-3-one with three protons, two in α position and one in α′ position gave thietanone 17.



17

F : The presence of four protons, three α and one α′, eg. ketone 18 gives the chlorothietanone 19 (21).

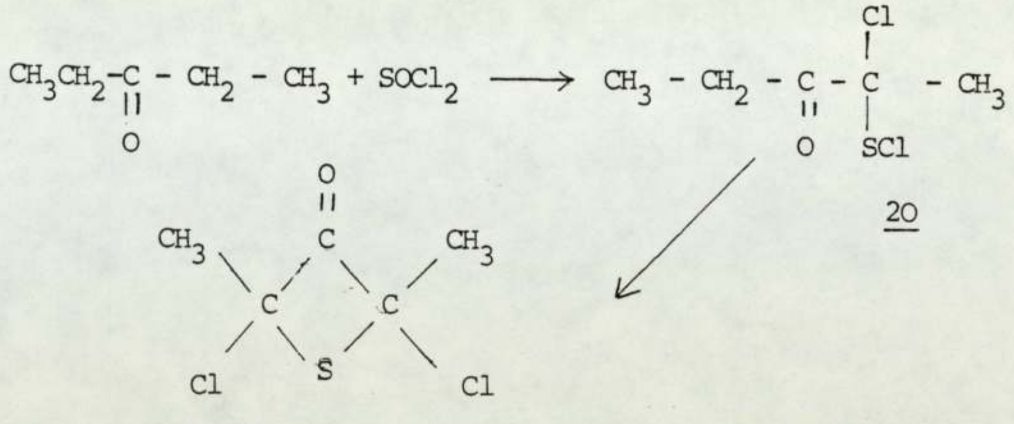


18

19

We studied the reaction of diethyl ketone with thionyl chloride. Diethyl ketone on treatment with thionyl chloride gave the α-chloro-α-sulfenyl chloride 20.

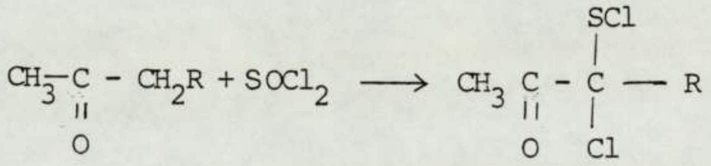
The α-chloro-α-sulfenyl chloride 20 in the presence of pyridine and on heating gave the dichlorothietanone 21.



20

21

G : Ketones possessing two α-protons and three α′ protons on treatment with thionyl chloride at room temperature give the α-chloro-α-sulfenyl chloride 22. The α-chloro-α-sulfenyl -chloride 22 with excess of thionyl chloride and a small amount of pyridine gave the chlorothietanone 23.

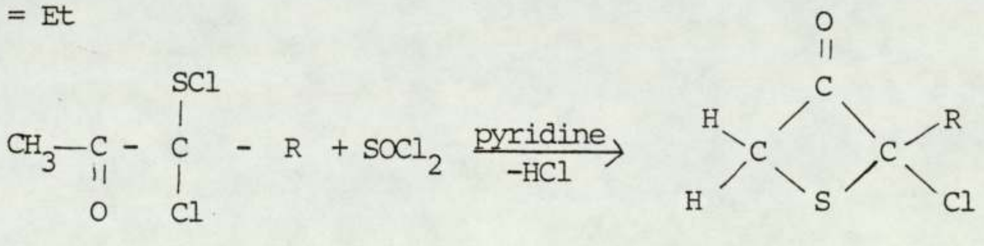


$CH_3-\underset{\underset{O}{\|}}{C}-CH_2R + SOCl_2 \longrightarrow CH_3\,\underset{\underset{O}{\|}}{C}-\overset{\overset{SCl}{|}}{\underset{\underset{Cl}{|}}{C}}-R$

22

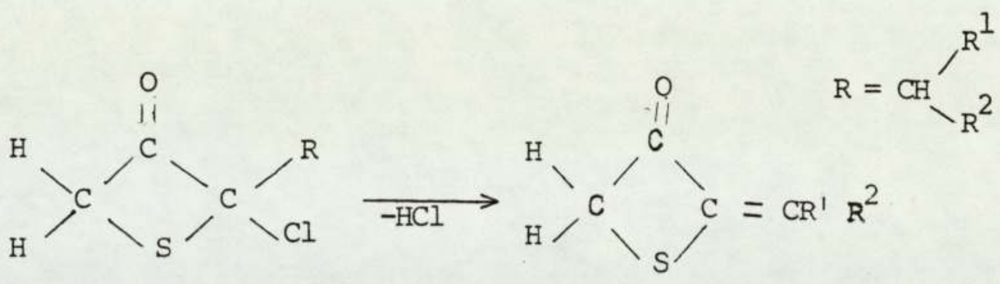
$R = CH_3$ $R = Me_2CH$

$R = Et$



23

Krubsack and Higa (22) prepared a number of thietan-3-ones 23 from the reaction of 4-substituted butan-2-ones with thionyl chloride. If R in 23 has a proton, it will lose hydrogen chloride to form 24.



23

24

This reaction was studied (18,20) with the following R^1 and R^2 groups

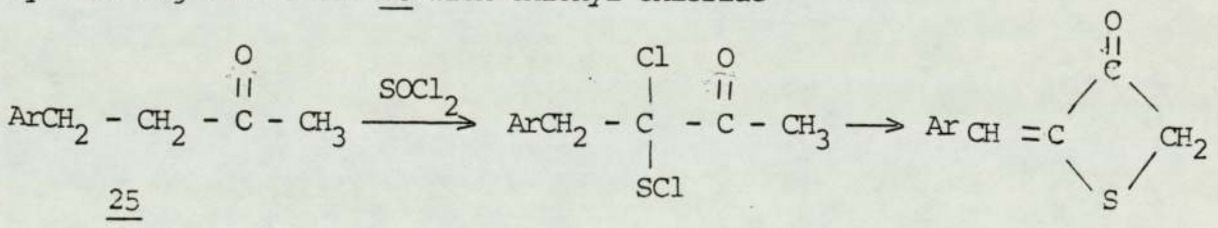
$R^1 = R^2 = CH_3$

$R^1 = H \quad R^2 = (CH_3)_2CH$

$R^1 = Ph \quad R^2 = Ph$

$R^1 = H \quad R^2 = Ph$

Krubsack et al.(23) attempted to study the mechanism of the reaction, by treating the ketone 25 with thionyl chloride



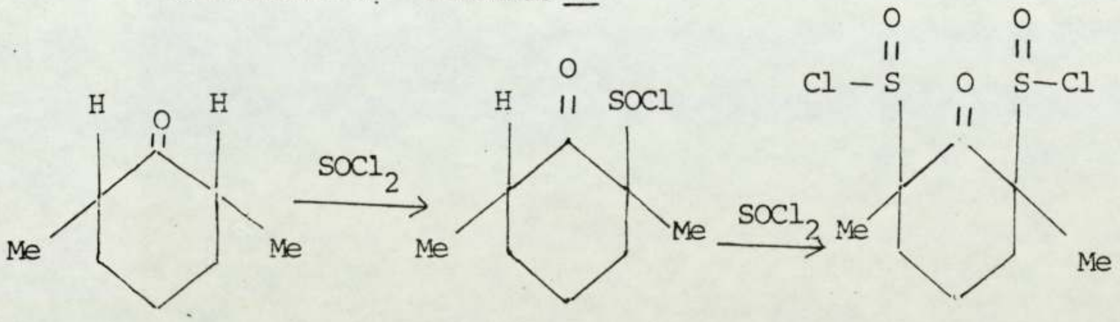
25

$Ar = 3\text{-}O_2N\,C_6H_4 \qquad Ar = 3 - F\,C_6H_4 \qquad Ar = 4 - O_2NC_6H_4$

H : The presence of 6 protons, three α and three α′, in a ketone gives(24) complex polymeric products, possibly due to the availability of six protons all equally active. Finally the cyclic ketone -2,6-dimethyl cyclohexanone with thionyl chloride gave (18) the disulfinyl chloride 27.

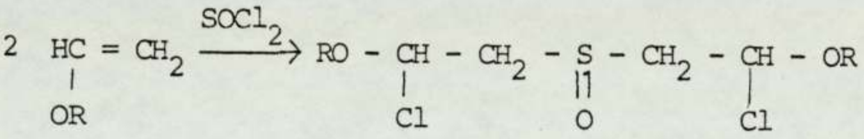
Pizey and Symeonides(18) isolated the monosulfinyl chloride 26.

The monosulfinyl chloride 26 with excess of thionyl chloride gave the disulfinyl chloride 27.



26 27

Addition of thionyl chloride to unsaturated compounds gives a variety of products, depending upon the structure of the alkene and the conditions employed. A number of enol ethers have been reported to produce β-chloro sulfoxides 28(25).



$$2\ \underset{\displaystyle OR}{\underset{|}{HC}} = CH_2 \xrightarrow{SOCl_2} RO - \underset{\displaystyle Cl}{\underset{|}{CH}} - CH_2 - \underset{\displaystyle O}{\underset{||}{S}} - CH_2 - \underset{\displaystyle Cl}{\underset{|}{CH}} - OR$$

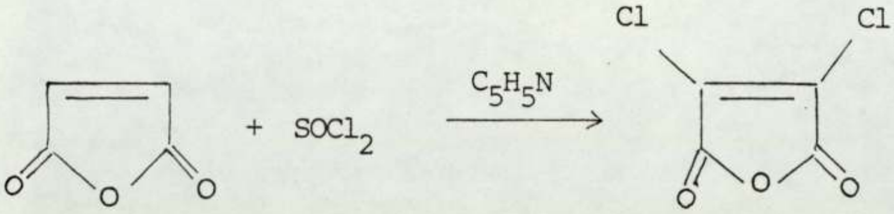
28

Patai and Patchornik(26,27) have studied the reaction of -1,1-diarylethylenes with thionyl chloride. The 1,1-diarylethylene 29 with thionyl chloride gives the 1,1-diarylvinyl chloride 30.

$$Ar_2C = CH_2 + SOCl_2 \longrightarrow Ar_2C = CHCl$$

29 30

Treatment of maleic anhydride with thionyl chloride in the presence of pyridine gave dichloromaleic anhydride (28).



Gladshtein et al.(29) have studied the reaction of 1,1-dichlorothylene with thionyl chloride.

$$CH_2 = CCl_2 + SOCl_2 \xrightarrow[0 - 5^{o}]{CCl_4} CCl_3{-}CH_2{-}SOCl$$

1 - b : Preparation and stereochemistry of the sulfinyl chlorides

Sulfinyl chlorides have been prepared by a number of different methods (30-34). Barnard (30) has prepared benzenesulfinyl chloride from the reaction of benzene with thionyl chloride.

$$C_6H_6 + SOCl_2 \longrightarrow C_6H_5\ SOCl$$

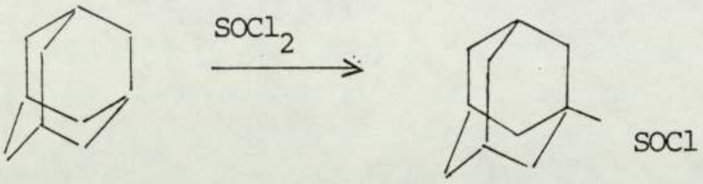
Primary and secondary alkylsulfur trichlorides ($RSCl_3$) were treated under controlled conditions with water to yield alkanesulfinyl chlorides (31). The sulfonyl chlorides 31 with thionyl chloride gave sulfinyl chlorides 32

$$\underset{\underline{31}}{R\ SO_2Cl} \xrightarrow{SOCl_2} \underset{\underline{32}}{R\ SOCl}$$

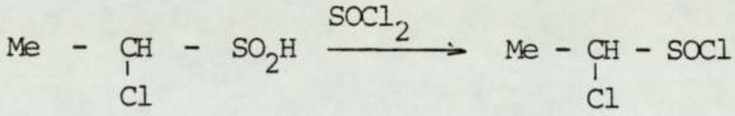
Treatment of 1,1-dichlorodimethyl sulfoxide <u>33</u> with chlorine gave sulfinyl chloride <u>34</u> (32).

$$\underset{\underline{33}}{Cl_2CH - SOCH_3} \xrightarrow[Cl_2]{CH_2Cl_2} \underset{\underline{34}}{CH_3SOCl} \quad 75\% \; + \; CH_3SO_2Cl \quad 1\%$$

Steeter et al.(33) prepared adamantane-1-sulfinyl chloride from the reaction of adamantane with thionyl chloride.



King and Beatson(34) reported that 1-chloroethanesulfinyl chloride at room temperature shows a nuclear magnetic resonance spectrum typical of a mixture of two diastereoisomers, due to the presence of two asymmetric centres. This was the first evidence of optical stability for the sulfinyl chloride group.



$$Me - \underset{Cl}{CH} - SO_2H \xrightarrow{SOCl_2} Me - \underset{Cl}{CH} - SOCl$$

Canalini et al.(35) have studied the nuclear magnetic resonance of the sulfinyl chlorides <u>35</u>.

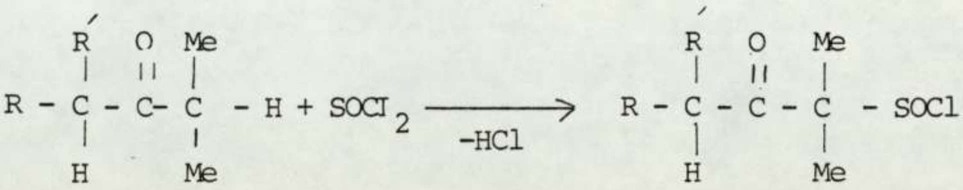
RCX_2 - SOCl   I $x = CH_3$ $R = H$

<u>35</u>   II $x = H$ $R = CH_3$

III $x = H$ $R = C_6H_5$

They have found non-equivalence of the CH_3, H group in isopropane I and ethane II sulfinyl chlorides.

The property of non-equivalence is solvent and temperature dependent. The isopropyl-β-ketosulfinyl chlorides 37 were prepared in high yields by treating the isopropyl ketones 36 with thionyl chloride under mild conditions (36).



$$R-\overset{R'}{\underset{H}{C}}-\overset{O}{\overset{\|}{C}}-\overset{Me}{\underset{Me}{C}}-H + SOCl_2 \xrightarrow[-HCl]{} R-\overset{R'}{\underset{H}{C}}-\overset{O}{\overset{\|}{C}}-\overset{Me}{\underset{Me}{C}}-SOCl$$

36 37

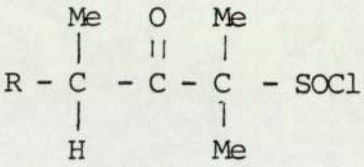
$R = CH_3 \quad R' = CH_3$

$R = H \quad R' = H$

$R = C_6H_5 \quad R' = H$

$R = CH_3 \quad R' = H$

The formation of the isopropyl-β-ketosulfinyl chlorides 37 appears to depend on the presence of the keto group or enol function. Thus isobutyronitrile and isopropyl acetate do not react with thionyl chloride under similar mild conditions. This suggests that the reaction proceeds via an enolic structure rather than via a carbanion type intermediate. The S-O stretching frequencies are known (37) to differ in different compounds. The sulfoxide absorption of sulfinyl (V_{SO}) in infrared spectra has been reported (36, 38) to be a strong band at 1150 ± 5 cm^{-1}. The nuclear magnetic resonance spectra (NMR) of isopropyl-β-ketosulfinyl chlorides 37 has been studied using variable temperature techniques and various solvents (39). The nuclear magnetic resonance (NMR) spectra studied showed that the relative chemical shifts of both the possible diastereotopic R and Me groups are temperature and solvent dependent and hence are due not only to the intrinsic diastereomerism of the group but also to conformational preferences (39).

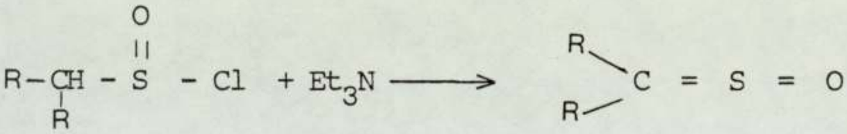


$$R-\overset{Me}{\underset{H}{C}}-\overset{O}{\overset{\|}{C}}-\overset{Me}{\underset{Me}{C}}-SOCl$$

R = H

R = CH_3

The reaction of the sulfinyl chlorides with amines was studied by Sheppard and Diekmann(40), Gupta and Pizey(41). Treatment of the sulfinyl chloride 38 with triethyl amine gave 39.

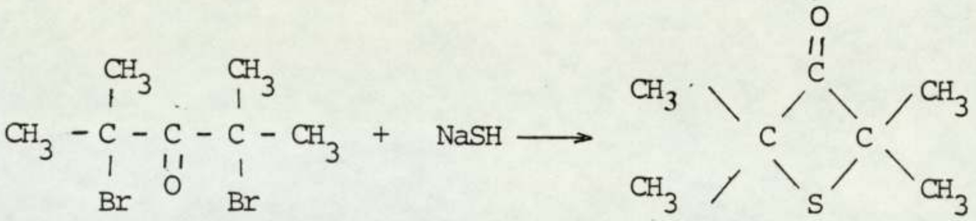


38 39

The sulfinamides were obtained from the reaction of sulfinyl chlorides with amines. The aliphatic, cyclo-aliphatic and aromatic ketones containing an α-isopropyl moiety could readily be converted to the α-sulfinyl chloride on treatment with thionyl chloride and then the sulfinyl chloride gave the β - ketosulfinamide on treatment with amine(41).

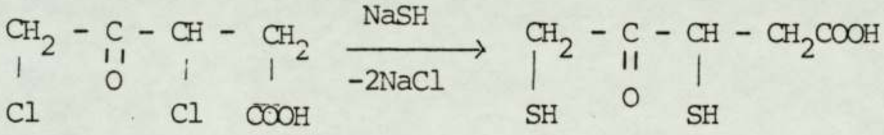
1 - c : The chemistry of thietan-3-ones

Since 1961, there have been unsuccessful attempts to synthesize thietan-3-one and derivatives of thietan-3-one in good yields. The reason for the difficult synthesis may be due to the high ring strain associated with these compounds. Claeson et al.(42) however, has reported the synthesis of-2,2,4,4-tetramethylthietan-3-one He found the reaction of α, ά - dibromodi -isopropyl ketone with sodium hydrosulfide gave-2,2,4,4-tetramethylthietan-3-one not the α-mercaptoketone as expected(42).



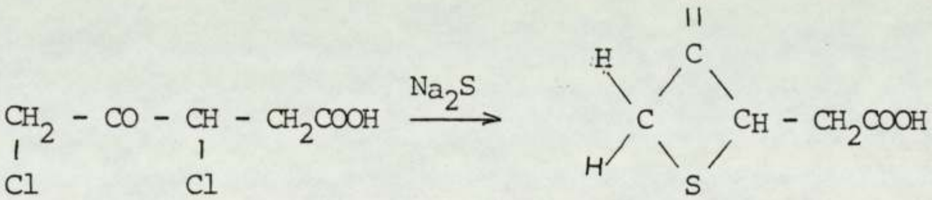
10

This method is not reported to be a general method for the synthesis of derivatives of thietan-3-one. Using this method he was not able to synthesize other derivatives of thietan-3-one(42). For example, when dichlorolevulinic acid 40 was treated with sodium hydrosulfide the dithiol 41 was obtained(43).



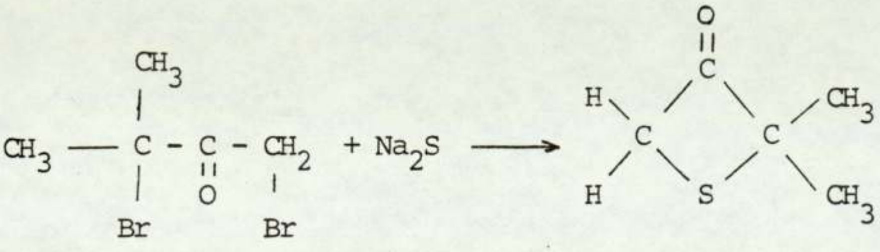
40 41

The treatment of dichlorolevulinic acid 40 with sodium sulfide gave the thietanone 42 in low yield.



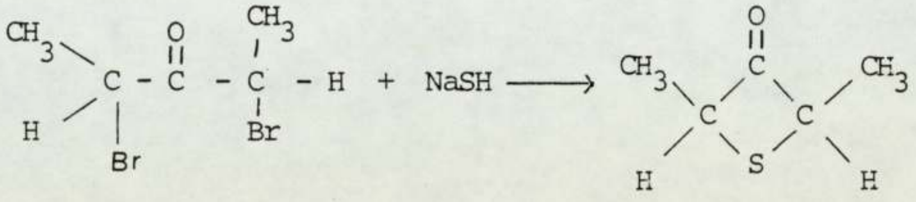
40 42

Luhmann et al.(44) have reported the synthesis of the thietanone 44 in low yield from the reaction of the α, ά dibromoketone 43 with sodium sulfide

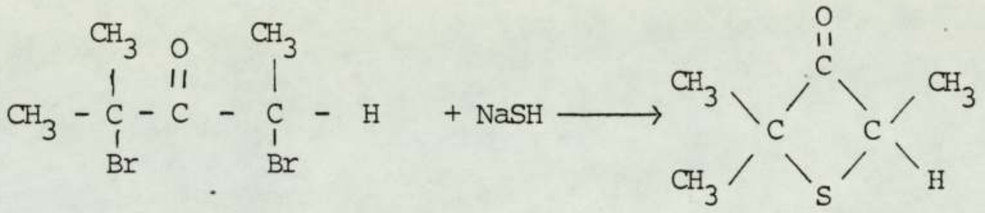


43 44

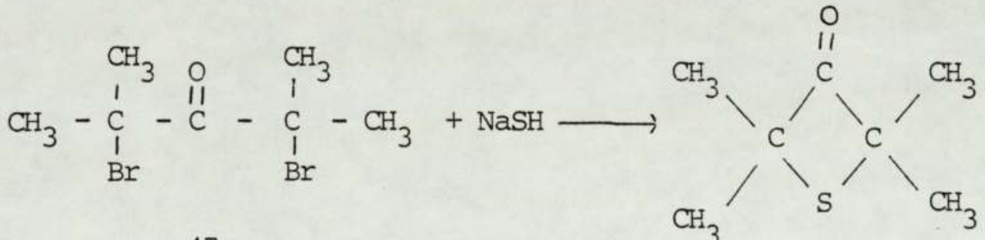
2, 4-dimethyl- 2, 2, 4-trimethyl- and-2,2, 4,4-tetramethylthietan-3-one have been synthesized in low yield from the reaction of the α, ά-dibromo ketones (45,46, 47) with sodium hydrosulfide(45, 46). Fohlisch and Czauderna(45) found the unsubstituted thietan-3-one and its-2-methyl derivative could not be obtained from the corresponding dibromo-ketones.



45



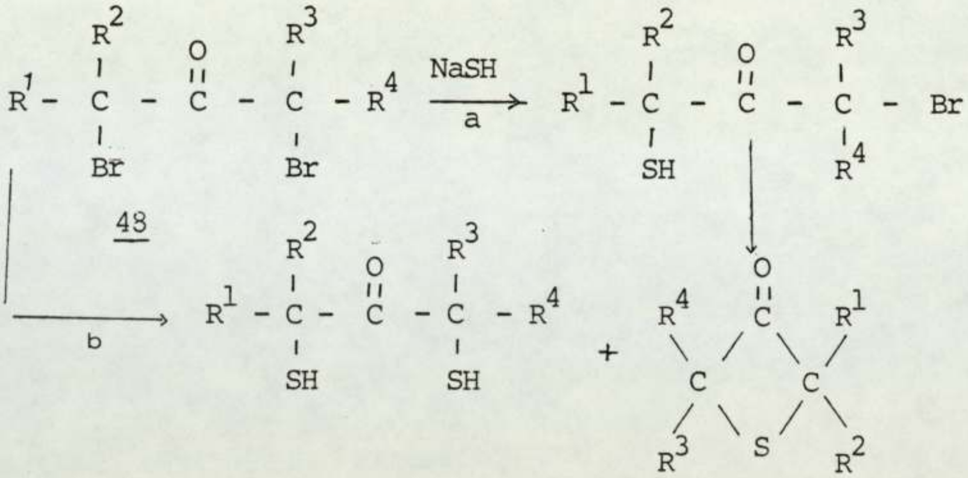
46

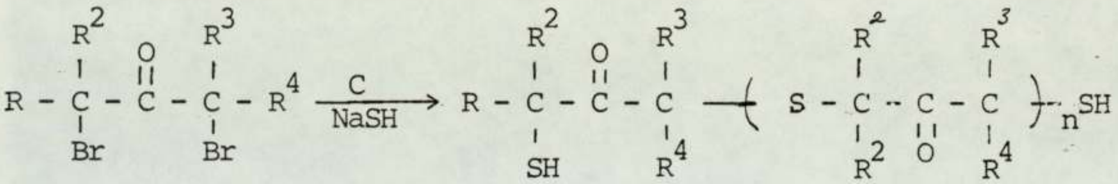


47

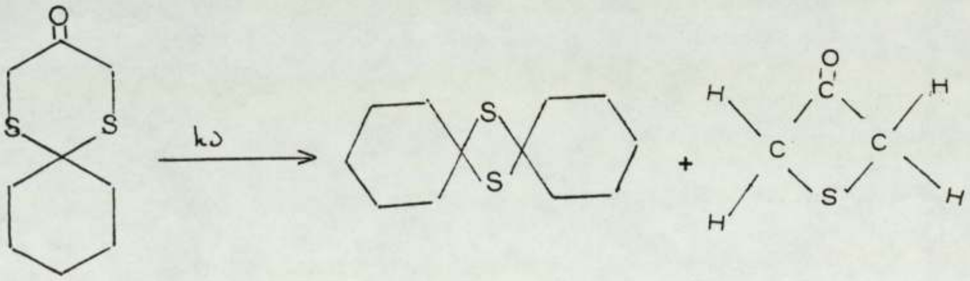
10

The reaction of the α, ά-dibromoketone 48 with sodium hydrosulfide can proceed by three different routes a, b, and c depending on the structure of the ketone.

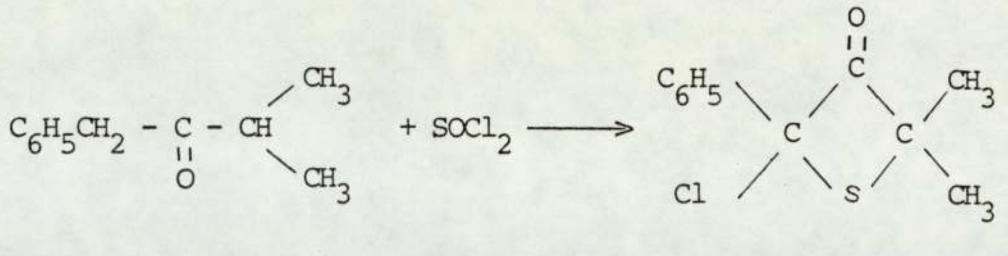




Irradiation of the 1,3-dithiacyclohexan-5-one in acetonitrile produced thietan-3-one in 21% yield$^{(47)}$.

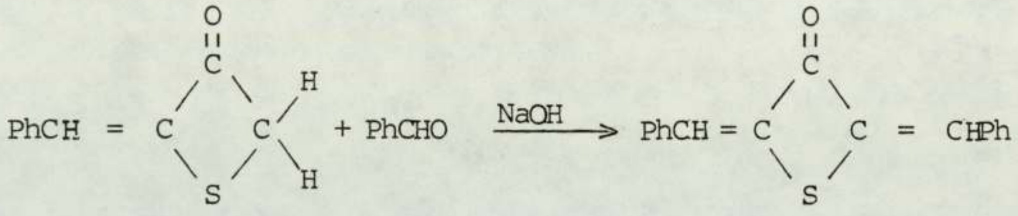


Pizey and Symeonides$^{(18, 36)}$ were able to isolate some derivatives of 2-chlorothietan-3-one from the reaction of certain ketones with thionyl chloride . Ketones containing three protons, one in a α and two in $\acute{\alpha}$ position usually give 2-chlorothietan-3-one . The minimum number of α, $\acute{\alpha}$ -protons for the formation of thietanone must be three protons for example benzyl isopropyl ketone with thionyl chloride gave the 2-chlorothietan-3-one 16.



16

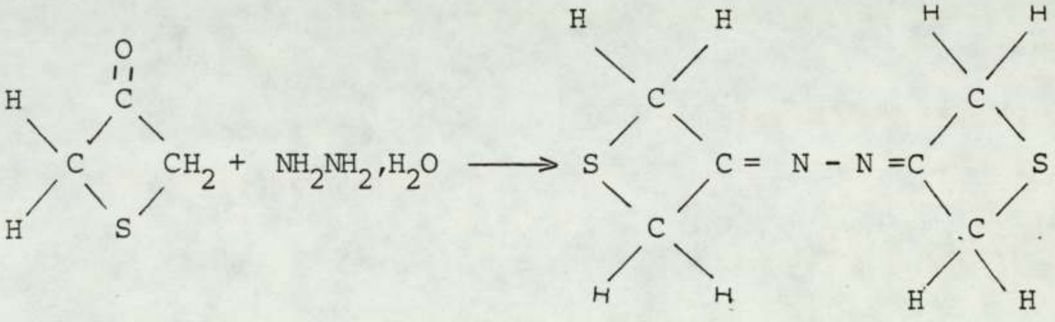
The electrophilic reaction of the thietan-3-one 49 with benzaldehyde yielded the thietan-3-one 50 (48).



49 50

Nucleophilic reactions of thietan-3-ones have been investigated by Seitz and Hoffmann (49) and Fohlisch and Gottstein (50). Seitz and Hoffmann (49) studied the reaction of the thietan-3-one with hydrazine hydrate and concluded that 51 is produced by the attack of hydrazine on the carbonyl group (C-3) of the thietan-3-one.

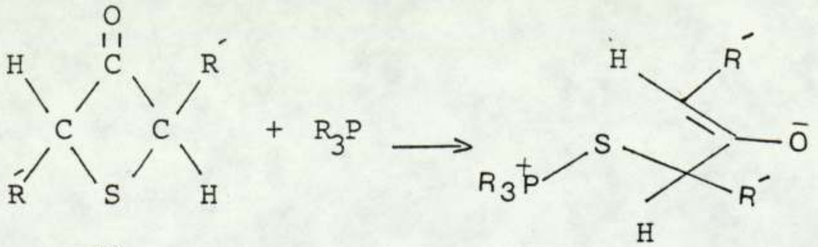
Scheme a



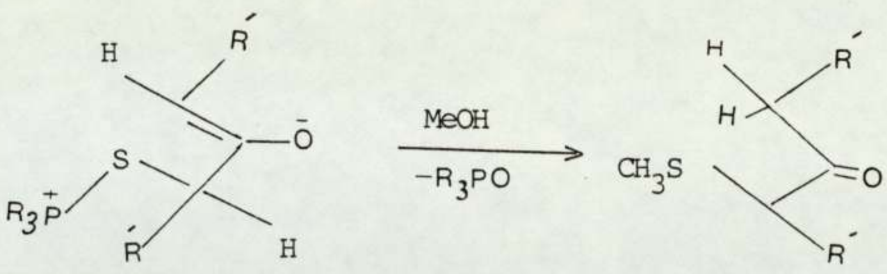
51

Fohlisch and Gottstein (50) found that the four-membered ring of 52 is cleaved by using triphenylphosphine in methanol and gives 53.

Scheme b



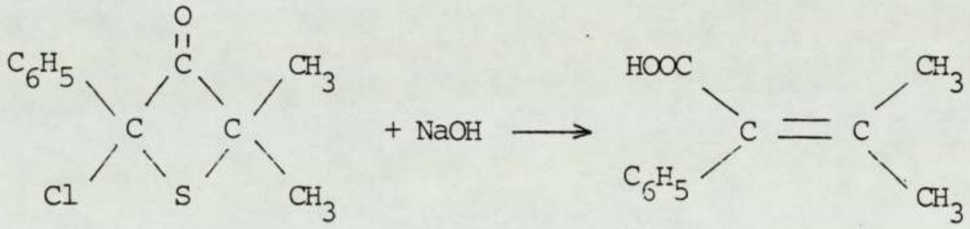
52



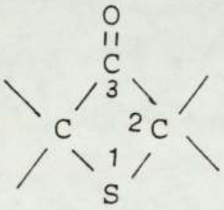
53

Scheme a and b described above may be rationalized in terms of nucleophilic attack of the hydrazine on the carbonyl (scheme a) and of the triphenylphosphine on the sulfur of the thietan-3-one (scheme b). This behaviour conforms with the hard and soft acid and base rule.

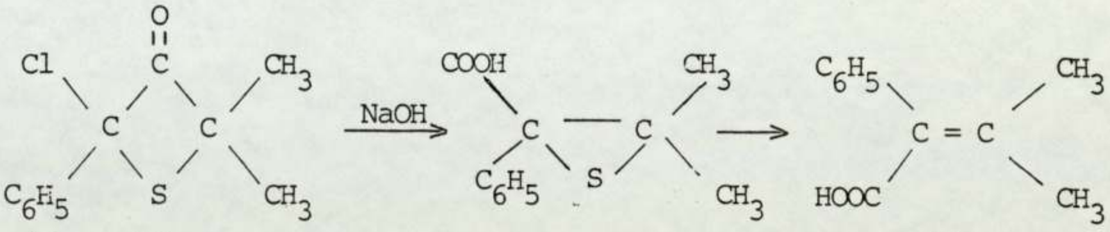
Treatment of the 2-chlorothietan-3-one 16 with sodium hydroxide gave the unsaturated carboxylic acid 54 (51).



16 54



The nucleophiles can attack carbon-2 or carbon-3 of the 2-chlorothietan-3-one 16. Sodium hydroxide is a hard base and therefore prefers to attack a hard acid (acceptor) according to Pearson(52, 53). Pearson(53) has shown that donor atoms with high electronegativity, small size, low polarizability and low oxidizability are hard bases. In contrast hard acids are those molecules which lack unshared electron pairs in their shell, have a small size and possess a high positive charge. The mechanism of the reaction of sodium hydroxide with 2-chlorothietan-3-one 16 is believed to follow the pathway suggested by Conia and Ripoll(54) for the reaction of 2-bromocyclobutan-1-one with hard bases.



16 54

The ring planarity of cyclobutane, cyclobutanone, oxetane, oxetan-3-one, thietane and thietan-3-one has been investigated(55-63). Far infrared and microwave spectroscopy were used to determine the structure of thietan-3-one. The effect of carbonyl substitution on the ring planarity and ring-puckering vibration has been analyzed by Meinzer et al.(64) who found that when a carbonyl group was present in a four membered ring planarity increased. This effect was rationalized in terms of strain energy for the planar conformation in which torsional repulsion and torsional interaction energy are at a minimum. Hence oxetan-3-one and thietan-3-one are more planar than oxetane and thietane.

The chemistry of four membered rings is almost unknown. The behaviour and the reactions of this class of compounds seem to be different from comparable linear molecules.

The object of this work was to study the chemistry of some novel derivatives of 2-chlorothietan-3-one. 2-Chlorothietan-3-ones have three reactive centres and so are useful intermediates for the preparation of a large number of new compounds which are difficult to synthesize by other methods. The reactions of derivatives of 2-chlorothietan-3-one with different nucleophiles have been studied.

The chlorination and reduction of the 2-chlorothietan-3-ones was also investigated. The structures of products were identified using infrared, nuclear magnetic resonance, mass spectroscopy and elemental analysis methods. The mechanisms of these reactions were studied by a variety of methods including nuclear magnetic resonance, electron spin resonance (esr) and chemical reactivity. The stereochemistry and planarity of these compounds was interpreted using nuclear magnetic resonance spectral techniques.

CHAPTER 2

PREPARATION AND REACTIONS OF NITRILE,KETONES AND DIBROMOKETONES

CHAPTER 2

CHAPTER TWO

SYNTHETIC EXPERIMENTAL

INTRODUCTION

This chapter deals with the experimental details of the preparative and synthetic chemistry, and includes the preparation of the ketones, dibromoketones, sulfinyl chlorides, sulfenyl chlorides, chlorothietanones, thiolanone, dithiolanones and aminothietanones.

The nuclear magnetic resonance spectra were run using 30, 60 or 90 MHz spectrometers, and tetramethylsilane (TMS) was always employed internally as the standard. The infrared spectra were recorded on a Perkin Elmer 237 spectrometer. Mass spectra were obtained using an AEI MS9 mass spectrometer. Unless otherwise stated, general purpose reagents and solvents were employed. Uncorrected melting and boiling points have been recorded.

2 - Preparation and reactions of nitrile, ketones and dibromoketones

2 - a: Preparation of isobutyronitrile.

Isobutyronitrile was prepared from the reaction of 2-chlorobutane with sodium cyanide in dimethyl sulfoxide(65).

Dimethyl sulfoxide was dried over a molecular sieve before use. Sodium cyanide was kept in an oven for two nights at 60-70°.

Sodium cyanide (60g) in dimethyl sulfoxide (300 ml) was heated to 90°. 2-Chlorobutane (92 ml, 1 mole) was slowly added to the solution of sodium cyanide in dimethyl sulfoxide . The reaction mixture was refluxed for three hours in an oil bath. The flask was then cooled, the reaction mixture was poured into water and the product was extracted using diethyl ether. The ethereal phase was washed several times with saturated sodium chloride solution, dried over calcium chloride, and the product was distilled after the diethyl ether was evaporated off to give isobutyronitrile.

b.p. = 40 - 42°/25 mm/Hg

(Lit. b.p. = 125 - 126°)[65]/760mm/Hg Yield = 69%.

IR (thin film)

2980(s) 2940(m) 2880(m) 2240(s) $C \equiv N$

1460(s) 1380(m) 1330(w) 1090(w)

1010(w) 965(m) cm^{-1}

NMR (CCl_4) 60 MHZ

δ	multiplicity	groups	integrals
0.7-2.0	multiplet	two methyl and methylene	8 protons
2.3-3.2	multiplet	methine	1 proton

2 - b: Preparation of the Ketones.

2 - b - 1: Benzyl isopropyl ketone.

The ketone (benzyl isopropyl ketone) was prepared by a method of Hauser and Renfrow(66) involving the reaction between a Grignard reagent (1 mole) and isobutyronitrile (1 mole).

A solution of benzyl chloride (1 mole) in anhydrous diethyl ether was slowly added to a mixture of magnesium metal (1.2 mole) in dry ether (60 ml). When the reaction had ceased isobutyronitrile (1 mole) was added slowly to the reaction mixture, and the resulting mixture was kept overnight at room temperature. It was then hydrolysed with excess 10N sulfuric acid. The mixture was then steam distilled. The organic layer was extracted by diethyl ether. The ether solution was dried with anhydrous sodium sulfate and the ether was removed using a rotary evaporator. The weight of the product was 120g. The product was then distilled under reduced pressure b.p. = 54°/0.05 mm/Hg yield = 75%. Lit b.p. = 220 - 221°/760mm/Hg.(67)

I.R. (thin film)

3075(w) 3040(m) 2980(w) 2980(s) 2940(w)
1710(s)(CO) 1600(w) 1495(m) 1455(m) 1380(w)
1040(s) 730(s) 690(s) cm^{-1}

NMR (in CCl_4)

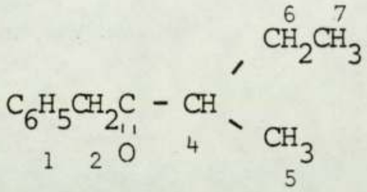
δ	multiplicity	integrals	groups
0.9	doublet	6 protons	methyl
2.4	septet	1 proton	methine
3.5	singlet	2 protons	methylene
7.2	singlet	5 protons	phenyl

2 - b - 2: 3-Methyl-1-phenylpentan-2-one

The reaction was carried out in a similar way to that described in 2 - b - 1. b.p. = 76 - 77°/0.08mm/Hg. Lit b.p. = 87 - 88°/3mm/Hg. (68)

I.R. (thin film)

3500(w) 3060(s) 3040(m) 2970(s)
2930(m) 2880(m) 1710(s) (C=O) 1600(w)
1500(s) 1450(s) 1380(m) 1200(m)
1050(s) 750(m) cm^{-1}



$C_6H_5CH_2C(=O)-CH(CH_2CH_3)CH_3$

NMR of 3-methyl-1-phenylpentan-2-one in CCl_4 and 90 MHz

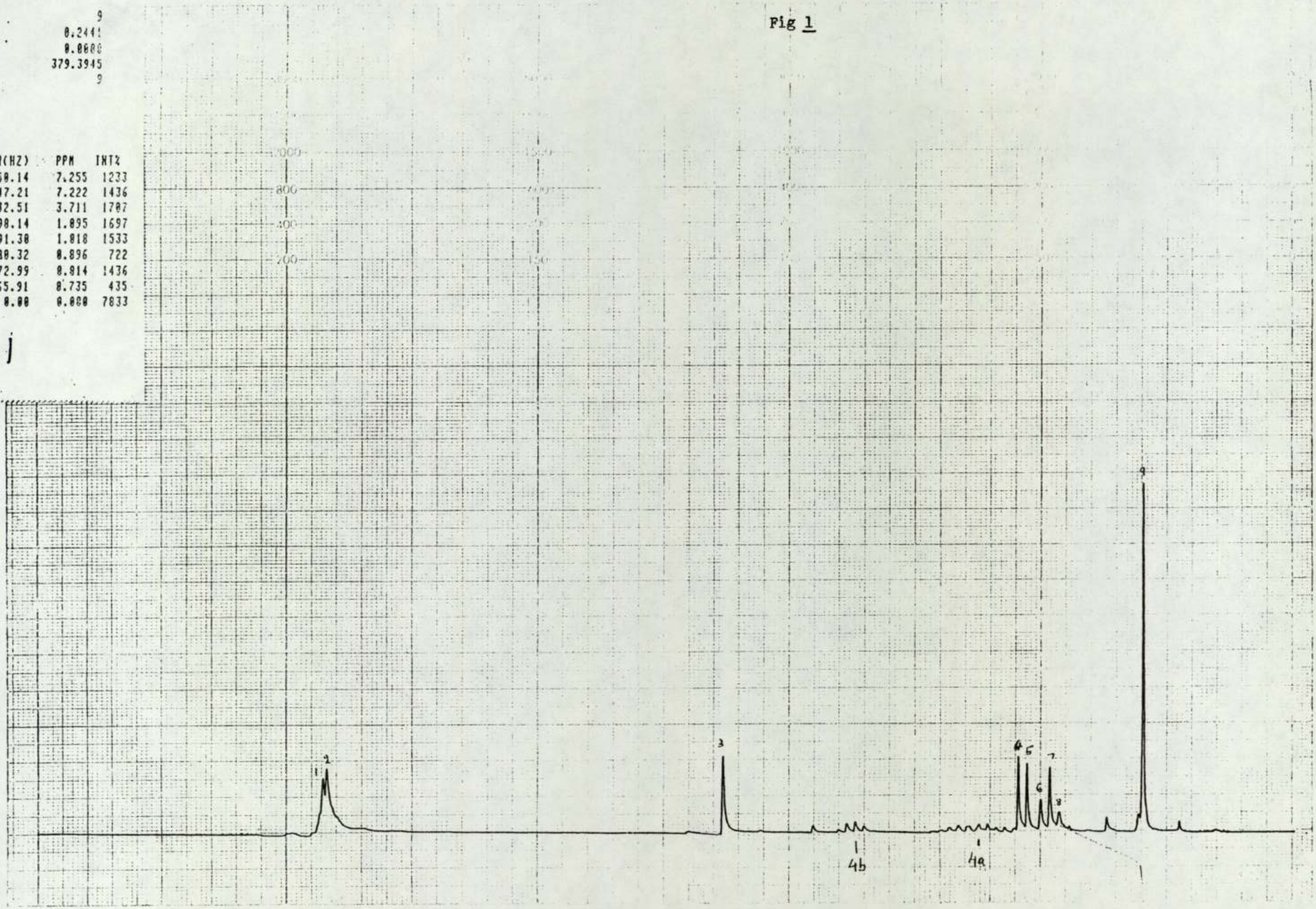
δ	groups	multiplicity	integrals
0.814	methyl (7)	triplet	3 protons
1.018-1.095	methyl (5)	doublet	3 protons
1.450	methylene (6)	multiplet	2 protons
2.548	methine (4)	multiplet	1 proton
3.711	methylene (2)	singlet	2 protons
7.200	phenyl	multiplet	5 protons

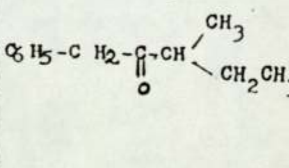
Figures 1, 2 and 3 show the ^1H and ^{13}C nuclear magnetic resonance spectrum of 3-methyl-1-phenylpentan-2-one from a Jeol FX-90 instrument.

Fig 1

```
AL          9
L      0.2441
F      0.0600
HZ   379.3945
IN          9

FREQ(HZ)   PPM   INT%
 650.14   7.255  1233
 647.21   7.222  1436
 332.51   3.711  1707
  98.14   1.895  1697
  91.30   1.818  1533
  80.32   0.896   722
  72.99   0.814  1436
  65.91   0.735   435
   0.00   0.000  7833
```




$C_6H_5-CH_2-\underset{\underset{O}{\|}}{C}-CH\begin{matrix}CH_3\\CH_2CH\end{matrix}$

SOLVENT CDCl$_3$
CONCENTRATION —
REFERENCE TMS
TEMPERATURE R.T.

NUCLEUS ^1H
OBS 89.55 MHZ
LOCK
IRR 89.55 MHZ
OFFSET
OBS 44.25
IRR 54.5
PULSE / SINGLE
WIDTH 10 —
INTERVAL —
REPETITION 5.0

DATA POINTS 8000/1K
WINDOW EX=0.12H$_3$T$_4$=4
NO. OF PULSES 10

SPECTRAL WIDTH 1000
RF GAIN —
AMPLITUDE 13

DECOUPLING NON
☐ CW ☐ NOISE
HOMO HETERO
POWER -
LOCK
RF LEVEL high 4
RF GAIN —
AMPLITUDE 22

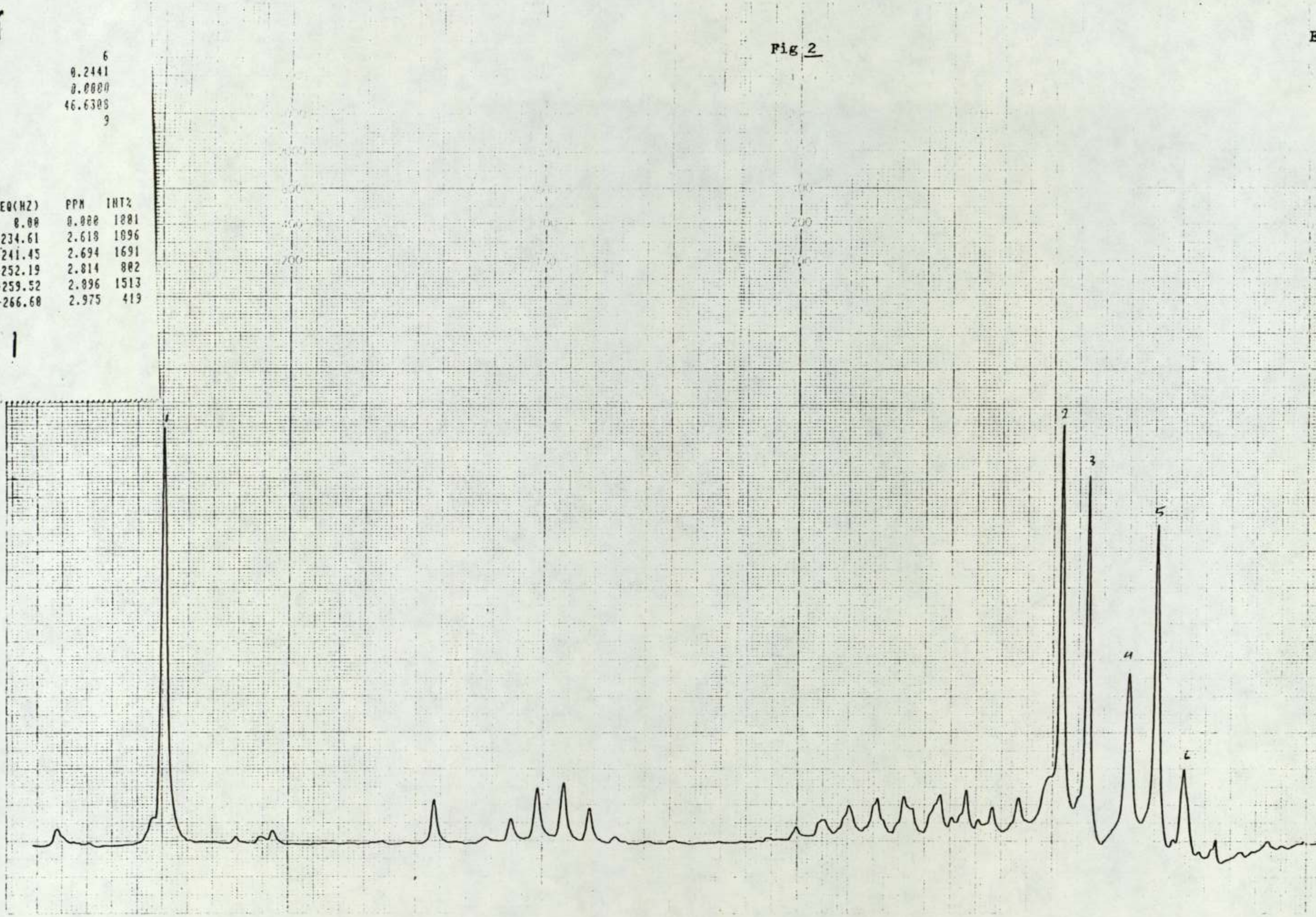
OPERATOR HAFID.

90QF7

Fig 2

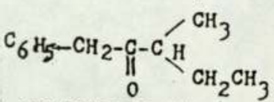
```
TOTAL            6
ESOL        0.2441
REF         0.0000
ESHZ       46.6308
GAIN             9

NO FREQ(HZ)     PPM   INT%
 1    0.00    0.000   1881
 2 -234.61    2.618   1896
 3 -241.45    2.694   1691
 4 -252.19    2.814    882
 5 -259.52    2.896   1513
 6 -266.68    2.975    419
```



Expanded spectrum of th

ketone



$C_6H_5-CH_2-\overset{\overset{O}{\|}}{C}-CH(CH_3)(CH_2CH_3)$

SOLVENT $CDCl_3$
CONCENTRATION —
REFERENCE NON
TEMPERATURE R.T.

NUCLEUS ^1H
OBS 89.55MHZ
LOCK
IRR
OFFSET
OBS 44.25
IRR 54.5
PULSE ☑ SINGLE
WIDTH 10
INTERVAL —
REPETITION 5.0

DATA POINTS 8000/IK
WINDOWEX=0.12H T =4
NO OF PULSES 10

SPECTRAL WIDTH 3330
RF GAIN —
AMPUTUDE 13

DECOUPLING NON
☐ CW ☐ NOISE
HOMO
POWER —
LOCK
RF LEVEL high 4
RF GAIN
AMPUTUDE 22

9th. June 19
HAFIP

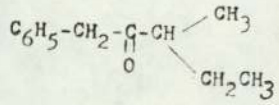
90 GFT

Fig 3

```
TAL           16
SOL       2.4414
EF        0.0000
HZ      827.6367
AIN           13

 FREQ(HZ)     PPM   INT%
   1853.82  82.246   939
    107.42   4.767   911
      0.00   0.000  6759
    -19.53   0.866  6482
5   -58.59   2.600  4083
6   -80.56   3.575   767
7 -1149.90  51.039  3367
8 -1181.64  52.447  3529
9 -1213.37  53.855  3276
10 -1823.73  80.946  4792
11 -1857.91  82.463  4375
12 -2060.54  91.457   554
13 -2333.98 103.594  3308
14 -2556.15 113.455  4111
15 -2656.25 117.898  4064
16 -2917.48 129.493  3486
```

①



$C_6H_5-CH_2-\underset{\overset{\|}{O}}{C}-CH\begin{smallmatrix}CH_3\\CH_2CH_3\end{smallmatrix}$

SOLVENT CDCl$_3$ TUBE 1 C
CONCENTRATION
REFERENCE - TMS
TEMPERATURE R.T.

NUCLEUS ^{13}C
OBS
LOCK /
IRR 89.55
OFFSET
OBS 33.0
IRR 54.5/SINGLE
PULSE
WIDTH 10
INTERVAL —
REPETITION 0.5

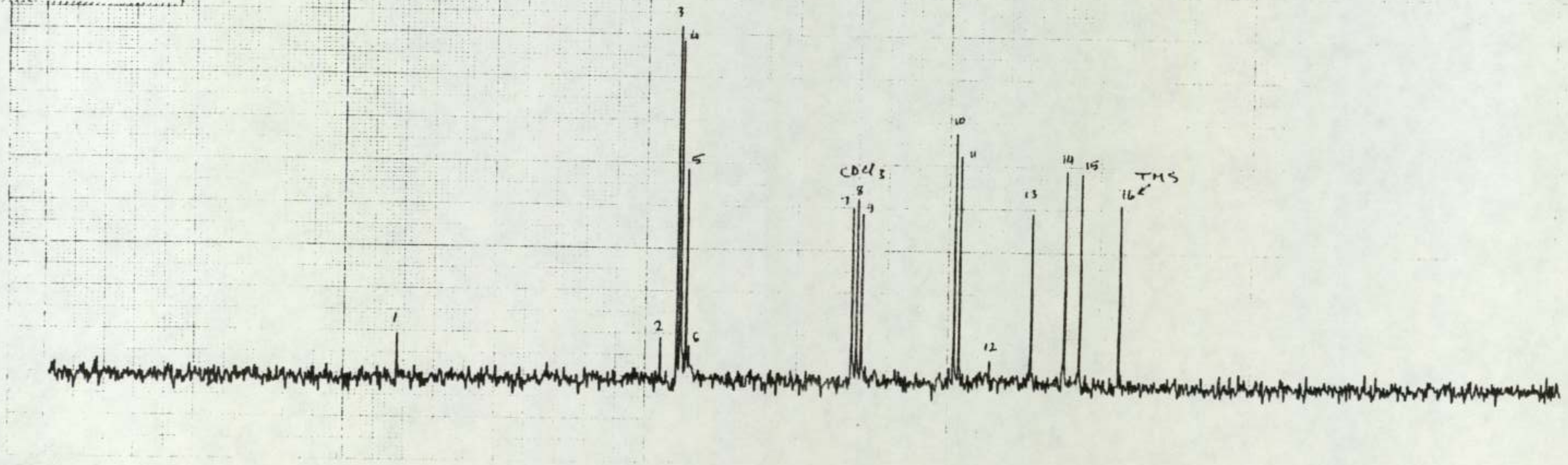
DATA POINTS 8000
WINDOW
NO OF PULSES 2500

SPECTRAL WIDTH 10000
RF GAIN
AMPLITUDE 17

DECOUPLING com
CW / NOISE
HOMO HETERO
POWER

A

DATE 23 9th June 81
OPERATOR HAF ID
REMARKS



2 - b - 3: 2-Methyl-5-phenylpentan-3-one.

2-Methyl-5-phenylpentan-3-one was prepared by a similar method to that used for benzyl isopropyl ketone (2-b-1). B.P. = 127/0.1mm/Hg.
An infrared spectrum showed a carbonyl group at 1710cms^{-1}.
NMR (in CCl_4) 30 MHz

δ	groups	multiplicity	integrals
7.2	Phenyl, C_6H_5	Singlet	5 protons
2.7	Methylene, C_6H_5 CH_2CH_2-	Singlet (b)	4 protons
1-0.8	Methyl	Doublet	6 protons
2.7 - 1.6	Methine	Septet	1 proton

2 - c: Preparation of the dibromoketones.

2 - c - 1: 1,3-Dibromo-3-methylbutan-2-one.

Bromine (254g, 1.55 mole) was slowly added to isopropyl methyl ketone (69g, 0.8 mole) in carbon tetrachloride (300 ml) at room temperature. The mixture was stirred overnight. Hydrobromic acid was removed by blowing a stream of nitrogen through the reaction mixture. Carbon tetrachloride was then evaporated and the resultant liquid was distilled to give 1,3-dibromo-3-methylbutan-2-one. b.P. = 86 - 88°/12mm/Hg.

Lit.b.p. = 99°/18mm, Hg$^{(69)}$
Lit.b.p. = 115°/15mm,Hg $^{(70)}$
Yield = 70%

calculated for $C_5H_8Br_2O$

C: 24.59   H: 3.2

found

C: 24.3   H= 3.2%

IR (Thin film)

2980 - 2920(m)   1720(s)(C=O) 1450(m)   1370(s)   1270(s) cm^{-1}

NMR (in CCl_4)   60 MHZ

δ	group	multiplicity	integrals
1.9	Methyl	Singlet	6 protons
4.4	Methylene	Singlet	2 protons

2 - c - 2: 1,3-Dibromo-3-methyl-1-phenylbutan-2-one(71-73).

Bromine (64g, 0.400 mole) was slowly added to benzyl isopropyl ketone (33.4g, 0.201 mole) in carbon tetrachloride (100 ml) at room temperature. The mixture was stirred for three hours. Hydrobromic acid was removed using nitrogen gas. The carbon tetrachloride was then evaporated off and the resulting solid was re-crystallized from methanol, to give 1,3-dibromo-3-methyl-1-phenylbutan-2-one.

m.p. = 53 - 55° yield = 85%

calculated for $C_{11}H_{12}Br_2O$

C: 41.25 H: 3.75

found

C: 41.50 H: 3.30 %

The mass spectrum showed a molecular ion peak at 320 mass units (table 1).

IR. (KBr disc)

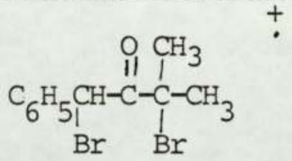
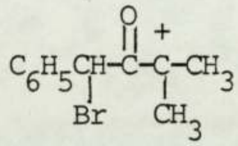
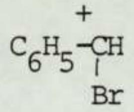
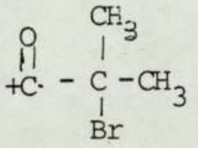
3080(w)	3020(s)	3000(w)	2980(w)
2920(w)	1710(s)C=O	1580(w)	1495(m)
1450(s)	1430(w)	1370(s)	1300(m)
1200(m)	1170(m)	1100(s)	1050(s)
1000(m)	700(s) cm^{-1}		

NMR (CCl_4) 60 MHZ

δ	groups	multiplicity	integrals
1.85	Methyl	Singlet	3 protons
2.05	Methyl	Singlet	3 protons
6.10	Methine	Singlet	1 proton
7.40	Phenyl	Singlet	5 protons

(Table 1)

Mass spectrum: 1,3-dibromo-3-methyl-1-phenylbutan-2-one.

$\frac{m}{e}$	Fragments	Relative intensity
318,320,322	 $C_6H_5CH(Br)-C(=O)-C(CH_3)(Br)-CH_3^{+\cdot}$	1 : 2 : 1
239,241	 $C_6H_5CH(Br)-C(=O)-\overset{+}{C}(CH_3)-CH_3$	1 : 1
170,171	 $C_6H_5-\overset{+}{C}H(Br)$	1 : 1
149,150	 $\overset{+}{C}(=O)-C(CH_3)(Br)-CH_3$	1 : 1
91	$C_6H_5-\overset{+}{C}H\cdot$	

2 - d : Purification of thionyl chloride$^{(74)}$

Triphenyl phosphite (80 ml) was slowly added to thionyl chloride (500 ml) and the mixture was distilled using a fractionating column. The main fraction distilled between 75° and 76° at room pressure, yield = 82%.

IR (thin film)

1343(w) 1232(s) cm^{-1}

2 - e.: Reactions of ketones with thionyl chloride.

2 - e - 1: Isopropyl methyl ketone.

Thionyl chloride (22 ml, 0.3 mole) was added dropwise to isopropyl methyl ketone (8.6g, 0.1 mole). The reaction mixture was stirred for eighteen hours at room temperature. Excess thionyl chloride was removed using a rotary evaporator.

The product was distilled to give 3-chlorosulfinyl-3-methylbutan-2-one b.p. = 56-58°/0.15mm/Hg yield = 80%, Lit. b.p. = 80°/3.5mm/Hg (21).

IR (thin film)

2980(w) 2930(w) 1700(s)(C=O) 1463(m) 1420(m)
1390(m) 1365(s) 1250(m) 1155(s)S=O 1110(s)
1015(w) 965(m) cm^{-1}

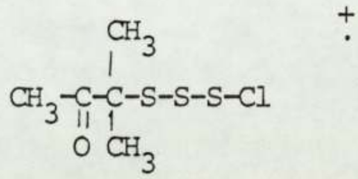
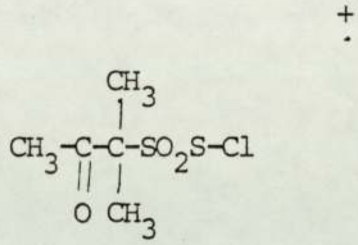
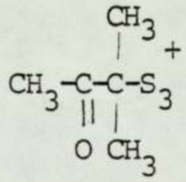
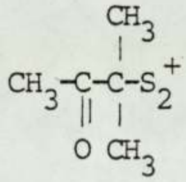
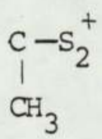
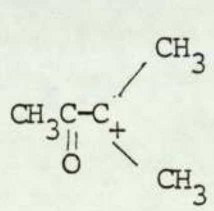
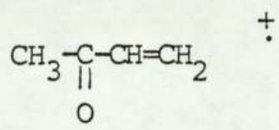
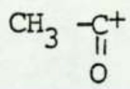
NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
2.3	Singlet	Methyl	3 protons
1.5	Singlet	Methyl	6 protons

The mass spectrum of 3-chlorosulfinyl-3-methylbutan-2-one did not give a molecular ion peak at 168 but showed peaks at $\frac{m}{e}$ 216, 218, 181, 183, 91, 85. (Table 2).

(Table 2)

Mass spectrum of 3-chlorosulfinyl-3-methylbutan-2-one.

m/e	Fragments
216, 218	 $CH_3-C(=O)-C(CH_3)_2-S-S-S-Cl^{+\cdot}$
216, 218	 $CH_3-C(=O)-C(CH_3)_2-SO_2S-Cl^{+\cdot}$
181	 $CH_3-C(=O)-C(CH_3)_2-S_3^+$
149	 $CH_3-C(=O)-C(CH_3)_2-S_2^+$
91	 $CH_3-C-S_2^+$
85	 $CH_3C(=O)-C^+(CH_3)_2$
70	 $CH_3-C(=O)-CH=CH_2^{+\cdot}$
43	 $CH_3-C^+(=O)$

2 - e - 2: Di-isopropyl ketone.

Di-isopropyl ketone (11.4g, 0.1 mole) was treated with thionyl chloride (22 ml, 0.3 mole). The reaction mixture was stirred overnight at room temperature. Excess thionyl chloride was removed using a rotary evaporator. The resultant liquid was distilled to give 2-chlorosulfinyl -2,4-dimethylpentan-3-one. (19.45g).

b.p. = 74 - 76°/0.8 mm/Hg yield = 78%

Lit. b.p. = 90-91°/1mm/Hg (21)

IR (thin film)

2980(s) 2940(m) (2880(w) 1695(s) C=O 1462(s)

1385(m) 1155(s) (S=O) 1080(s) 1020(s) cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.10	Doublet	Methyl	6 protons
1.65	Singlet (b)	Methyl	6 protons
3.15	Septet	Methine	1 proton

2 - e - 3: Diethyl ketone.

Diethyl ketone (8.6g, 0.1 mole) was slowly added to thionyl chloride (30 ml, 0.3 mole) at -5°. The reaction mixture was stirred at room temperature for one night. Excess thionyl chloride was then evaporated off using a rotary evaporator. The product was distilled to give 2-chloro-2-chlorosulfenylpentan-3-one b.p. = 78°/4.5 mm/Hg yield = 70%.

IR (thin film)

2990(m) 2940(m) 1720(s)C=O 1440(m) 1370(m)
1340(w) 1160(s) 1080(s) 960(w) cm^{-1}

NMR (CCl_4) 30 MHz

δ	groups	multiplicity	integrals
3.00	Methylene	Quartet	2 protons
2.15	Methyl	Singlet	3 protons
1.15	Methyl	Triplet	3 protons

2 - e - 4: Diethyl ketone in the presence of pyridine.

Diethyl ketone (8.6g, 0.1 mole) and pyridine (15 drops) were slowly added to thionyl chloride (22 ml, 0.3 mole) at room temperature in the dark under nitrogen gas.

The mixture was stirred at 35 - 40° for one day. The excess of thionyl chloride was evaporated off using a rotary evaporator at 30°. Ether (30 ml) was added to the resulting liquid. The precipitate was filtered off and the ether was then evaporated. The product was distilled to give <u>2,4-dichloro-2,4-dimethylthietan-3-one</u>. m.p. = 40-42° yield = 20%. The majority of the product decomposed during distillation.

IR (thin film)

2930(m)	2985(m)	2860(w)	1795(s) C=O
1620(b)	1440(s)	1380(s)	1170(w)
1070(s)	970(m)	800(s)	750(s) cm^{-1}

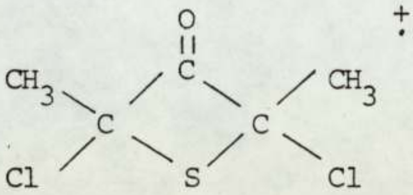
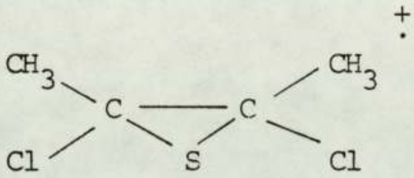
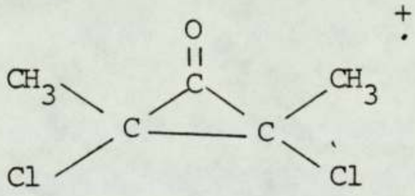
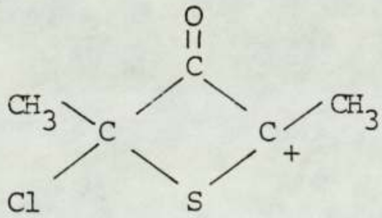
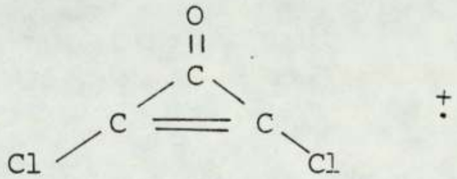
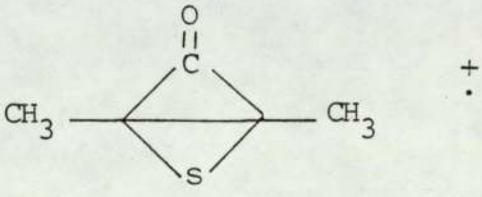
NMR (CCl_4) 30 MHz

δ	groups	multiplicity	integrals
2.35	Methyl	Singlet	3 protons
2.20	Methyl	Singlet	3 protons

The relative intensity of the two singlet peaks at δ = 2.35 and δ = 2.20 ppm in the nuclear magnetic resonance spectrum was almost 3:2. The mass spectrum of 2,4-dichloro-2,4-dimethylthietan-3-one showed molecular ion peaks at 184, 186 and 188. When the reaction mixture was heated for 5 days at 35°, the product was collected at a pressure of 0.001 mm/Hg at 22° and the melting point was 47 -50°, and the relative intensity of the two singlet peaks at δ = 2.35 and 2.2 ppm was 7:3 in NMR spectrum. Two peaks at δ = 2.35 and 2.2 ppm are due to methyl protons of cis- and trans- isomers of 2,4-dichloro-2,4-dimethylthietan-3-one.

(Table 3)

Mass spectrum of 2,4-dichloro-2,4-dimethylthietan-3-one

Mass ions	Fragments
184, 186, 188	
156, 158, 160	
152, 154, 156	
149, 151	
122, 124, 126	
114	

Mass spectrum of 2,4-dichloro-2,4-dimethylthietan-3-one showed the intensity ratio of peaks 184, 186, 188 to be 10 : 6 : 1 which confirmed the existence of two chlorine atoms in the molecule.

Accurate mass spectra of 2,4-dichloro-2,4-dimethylthietan-3-one cf ions at m/e184, 186 and 188.

m/e	molecular formula	calculated molecular wt.	given molecular wt.	error
184	$C_5H_6{}^{35}Cl_2O\ S$	183.95000	183.95163	3.5 ppm
186	$C_5H_6{}^{35}Cl{}^{37}Cl\ O\ S$	185.94920	185.94868	2.7 ppm
188	$C_5H_6{}^{37}Cl_2\ O\ S$	187.94551	187.94573	1.1 ppm

2 - e - 5: Ethyl isopropyl ketone.

2 - e - 5a: Ethyl isopropyl ketone in the presence of pyridine at -50°.

Ethyl isopropyl ketone (8.6g, 0.1 mole) and pyridine (10 drops) were slowly added to thionyl chloride (22 ml) at -50°. The mixture was allowed to stand at 0° for eighteen hours. The excess of thionyl chloride was evaporated off at room temperature under vacuum. The product was kept at -80° for four days.

The solid compound was dissolved in carbon tetrachloride and the solution was then filtered. The carbon tetrachloride was evaporated at room temperature under vacuum. The red thick oil was kept in the cold (-80°) for a few days. The solid was filtered off and collected to give 2-chloro-2,4,4-trimethylthietan-3-one. m.p. = $35-40^{\circ}$ yield = 30%

IR (CCl_4)

3080(w)   2980(m)   1780(s)(C=O)   1640(m)   1490(m)   1260(s)

NMR (CCl_4)   30MHz

δ	multiplicity	groups	integrals
2.00	Singlet	Methyl	3 protons
1.85	Singlet	Methyl	3 protons
1.58	Singlet	Methyl	3 protons

2 - e - 5b: Ethyl isopropyl ketone in the presence of pyridine at 0°.

Ethyl isopropyl ketone (8.6g, 0.1 mole) and pyridine (0.2 ml) were slowly added to thionyl chloride (22 ml) at 0°. The mixture was stirred at room temperature for one day. The excess of thionyl chloride was evaporated and the product was then distilled to give 2,2-dimethyl-4-methylenethietan-3-one. b.P. = 60°/0.1mm/Hg.

IR (thin film)

3080(m)   2870(w) cm^{-1} 1760(s)(C=O)

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.65	Singlet	Methyl	3 protons
1.85	Singlet	Methyl	3 protons
4.00	Singlet	Methylene	2 protons

2 - e - 6: Benzyl isopropyl ketone.

3-Methyl-1-phenylbutan-2-one (benzyl isopropyl ketone) (30g, 0.18 mole) and pyridine (0.2 ml)were added dropwise to thionyl chloride (65 ml, 0.6 mole) and the reaction mixture was stirred for one week at 27 - 30° in the dark. The excess of thionyl chloride was removed under reduced pressure in a stream of nitrogen gas. Pyridine (0.5 ml) was then added to the resulting compound and ether was then added to the mixture. The pyridine hydrochloride was filtered off and the ether was then removed at room temperature using a rotary evaporator to give an 80% yield of 2-chloro-4,4-dimethyl-2-phenylthietan-3-one.

This reaction has been reported by Pizey and Symeonides$^{(36)}$ in the absence of pyridine. The mass spectrum of 2-chloro-4,4-dimethyl-2-phenylthietan-3-one showed a molecular ion peak at 226 (Table 4).

IR (thin film)

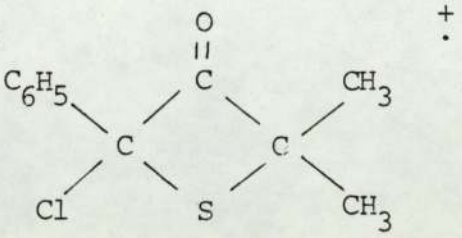
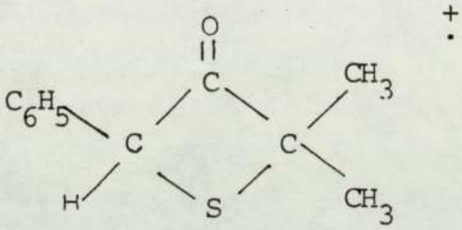
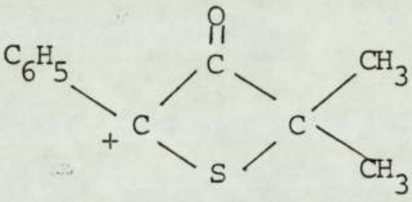
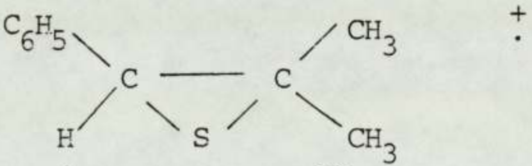
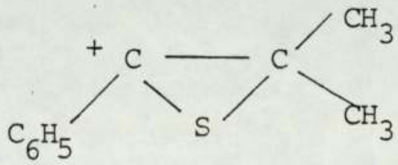
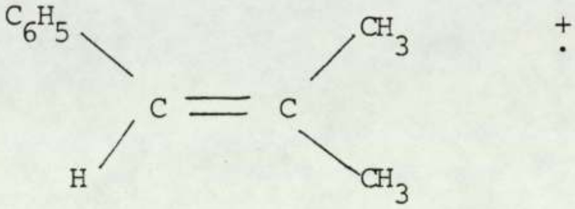
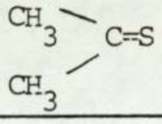
3060(w)	2980(m)	2920(m)	2860(w)	1780(s) (C=O)	
1500(w)	1450(m)	1365(m)	1380(w)	1120(m)	1050(m)
950(w)	860(m)	790(m)	740(s) cm^{-1}		

NMR (CCl_4) 30MHZ

δ	multiplicity	integrals	groups
1.40	Singlet	3 protons	Methyl
1.75	Singlet	3 protons	Methyl
7.35	Multiplet	5 protons	Phenyl

(Table 4)

Mass spectrum of 2-chloro-4,4-dimethyl-2-phenylthietan-3-one.

m/e	Fragments
226,228	
192	
191	
164	
163	
132	
77,74	$C_6H_5^+$  $(CH_3)_2C{=}S$

2 - e - 7: 3-Methyl-1-phenylpentan-2-one.

3-Methyl-1-phenylpentan-2-one (8.8g, 0.05 mole) and pyridine (3 drops) were added to thionyl chloride (12 ml) at room temperature.

The reaction mixture was stirred for eight days in the dark at 35 - 45°.

The excess of thionyl chloride was removed under low pressure and nitrogen gas to give 2-chloro-4-ethyl-4-methyl-2-phenylthietan-3-one. Yield of the crude product = 95%

IR (thin film)

3080(w)	3040(w)	2980(s)	2940(m)	2880(m)
2810(vw)	1790(s)C=O	1600(w)	1490(m)	1450(s)
1380(m)	1280(w) cm^{-1}			

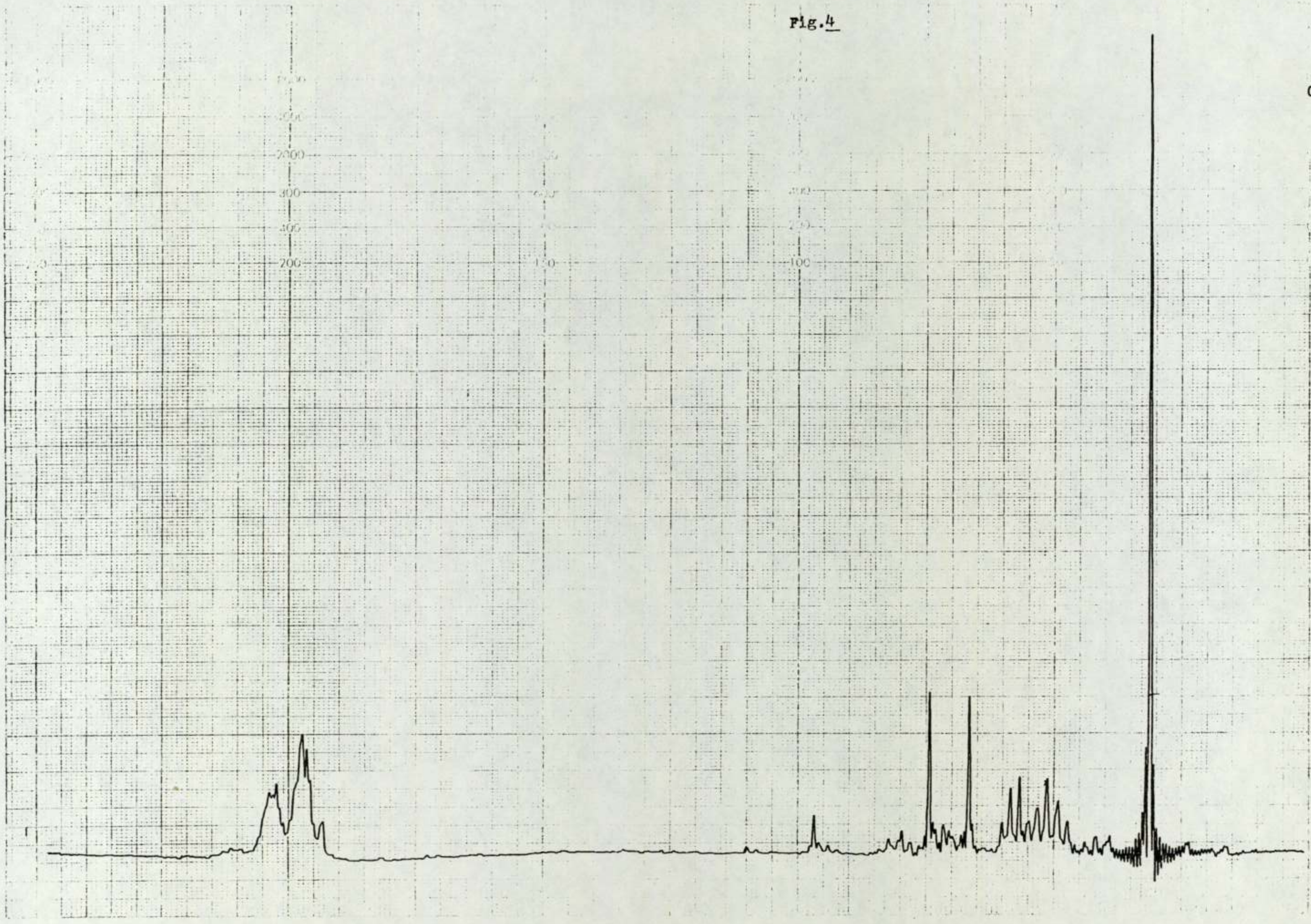
NMR (CCl_4) 60 MHz

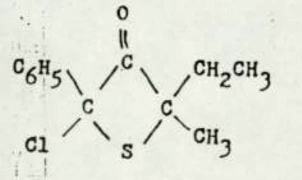
δ	multiplicity	groups
0.75 - 1.35	Multiplet	Ethyl
1.5 o	Singlet	Methyl(1)
1.9 o	Singlet	Methyl(2)
7.3 o	Multiplet	Phenyl

The relative intensity of protons of methyl(1) to methyl(2) is $^{82}/_{77}$ = 1.06.

Figures 4 and 5 show the ^{1}H and ^{13}C nuclear magnetic resonance spectra of 2-chloro-4-ethyl-4-methyl-2-phenylthietanone-3-one from a Jeol FX-90 instrument.

Fig.4





SOLVENT $CDCl_3$
CONCENTRATION
REFERENCE TMS
TEMPERATURE R.T.

NUCLEUS ^1H
OBS. LOCK 89.55
IRR 89.55
OFFSET
OBS. 44.25
IRR 54.5
PULSE SINGLE
WIDTH
INTERVAL
REPETITION

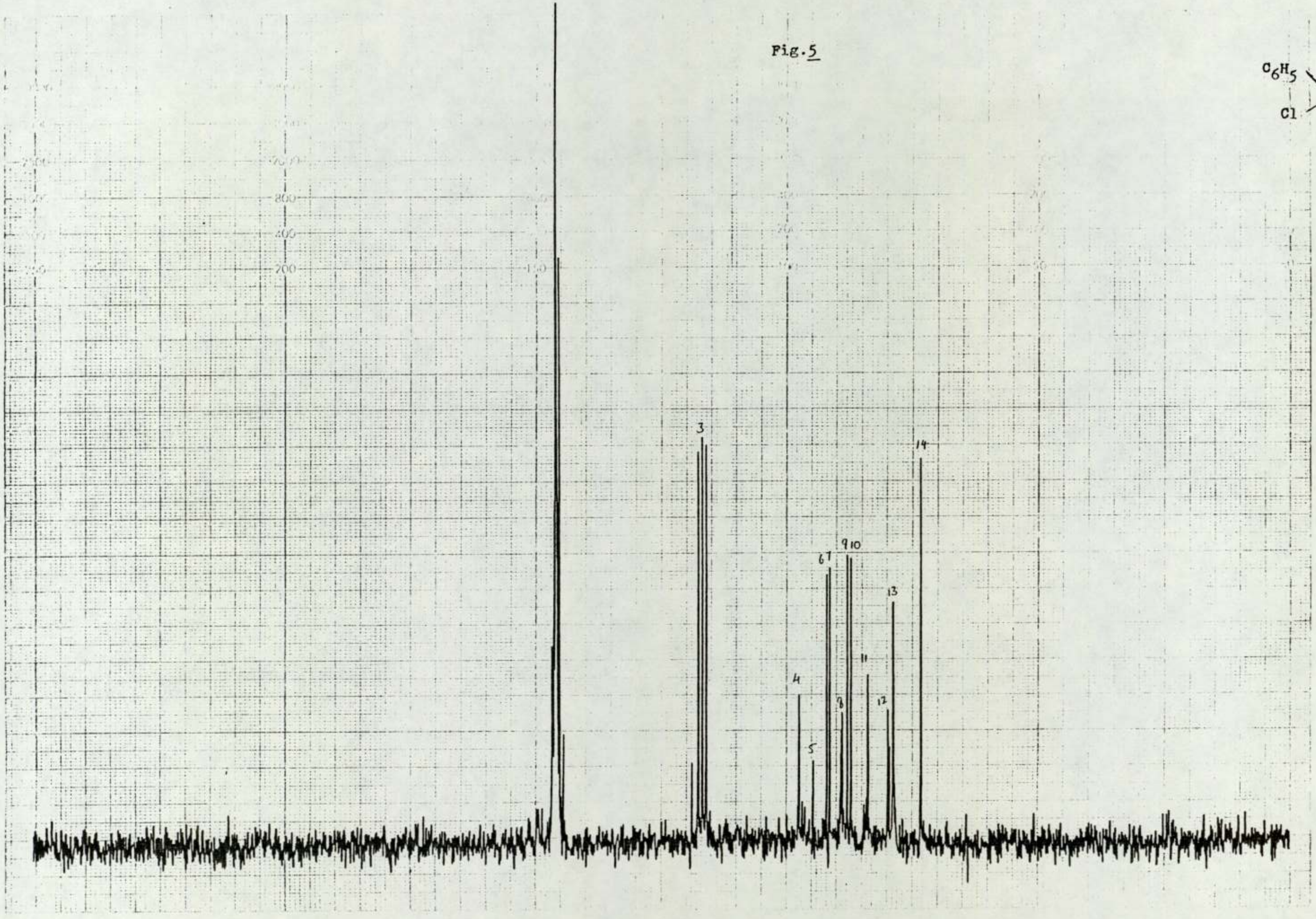
DATA POINTS 8000
WINDOW
NO OF PULSES 10

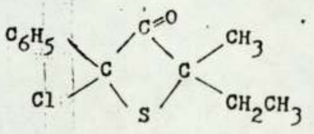
SPECTRAL WIDTH 1000
RF GAIN
AMPLITUDE 13

DECOUPLING NON
CW NOISE

90 a

Fig.5





SOLVENT CDCl3 ic
CONCENTRATION —
REFERENCE
TEMPERATURE R.T.

NUCLEUS ^{13}C
OBS 22.5
LOCK /
IRR 89.55
OFFSET
OBS 33.0
IRR 54.5
PULSE
WIDTH
INTERVAL —
REPETITION 0.5

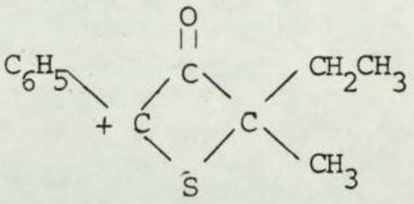
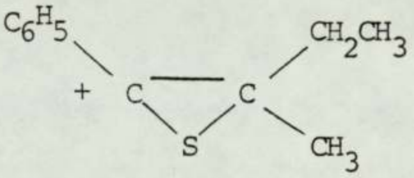
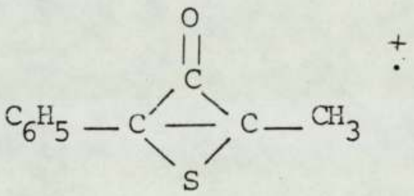
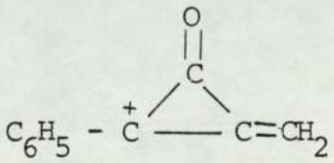
DATA POINTS 8000
WINDOW EX=6T4=4045
NO OF PULSES 5000

SPECTRAL WIDTH 10000
RF GAIN
AMPLITUDE 19

DECOUPLING com
CW /NOISE
HOMO HETERO
POWER
LOCK
RF LEVEL high 4
23
4.6.81

The mass spectrum of 2-chloro-4-ethyl-4-methyl-2-phenylthietan-3-one gave the ions at $\frac{m}{e}$ 408, 341, 294, 238, 205, 177, 178, 143, 121, 105. The possible structure of some mass ions have been worked out in Table 5.

Mass spectrum of 2-chloro-4-ethyl-4-methyl-2-phenylthietan-3-one (Table 5)

m/e	Fragments
205	
177	
178	
143	

2 - e - 8: 2-Methyl-5-phenylpentan-3-one.

2-Methyl-5-phenylpentan-3-one (10g, 0.06 mole) was added to thionyl chloride (18 ml). The mixture was stirred overnight at room temperature. Pyridine (1.5 ml) was added to the reaction mixture. The mixture was heated for four hours at 50-55°. Pyridine (0.5 ml) was added, the reaction mixture was heated for a further two hours. The excess thionyl chloride was evaporated off. The pyridine hydrochloride was quickly filtered off and the product was allowed to stand at 50° overnight. The resulting solid was kept for thirty minutes at room temperature. Then cold petroleum ether (40 - 60°) was added to the crystals. The crystals were filtered off and washed with cold petroleum ether (40 - 60°). The yellow crystals were 4-benzylidene-2,2-dimethylthietan-3-one, m.p. = 50 - 53° yield = 65%.
(Lit m.p. = 46 - 47° (18).

IR (CCl_4)

2980(m)	2920(w)	1755(s) (C=O)	1610(m)	1490(w)
1450(m)	1250(w)	1120(s)	1090(s)	950(w) cm^{-1}

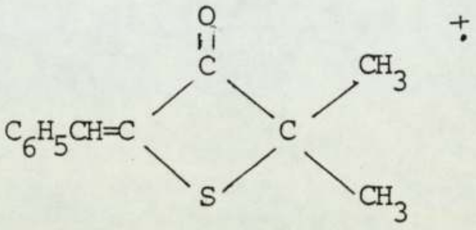
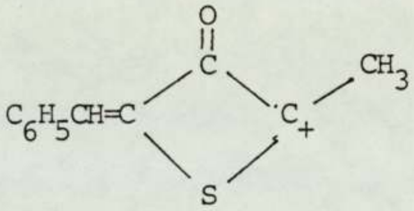
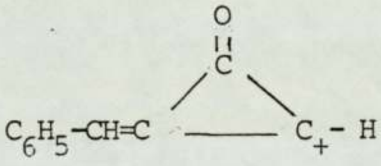
NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
7.45	Multiplet	Phenyl and Methine	6 protons
1.75	Singlet	Methyl	6 protons

The mass spectrum of 4-benzylidene-2,2-dimethylthietan-3-one showed a molecular ion peak at 204 mass units (Table 6).

(Table 6)

Mass spectrum of 4-benzylidene-2,2-dimethylthietan-3-one.

m/e	Fragments
204	
189	
143	
115	$C_6H_5CH=C=\overset{+}{C}H$
117	$C_6H_5-CH=\overset{+}{C}-CH_3$

Accurate mass spectrum of an ion at $\frac{m}{e}$ 204

m/e	Molecular formula	calculated molecular weight	given molecular wt.	error
204	$C_{12}H_{12}OS$	204.05143	204.06088	2.6ppm

2 - e - 9: Dibenzyl ketone.

Dibenzyl ketone (10g, 0.05 mole) and pyridine (0.2 ml) were heated to 60°. Thionyl chloride (15 ml, 0.2 mole) was added to the dibenzyl ketone at 60°. The reaction mixture was stirred for three days. The excess of thionyl chloride was then evaporated off and the resultant products were distilled.

b.p. = $90-100^{\circ}/0.07$mm/Hg.

Two fractions were obtained by redistillation.

Fraction (1) :

Fraction (1) was 2,4-diphenylthietan-3-one. Yield = 17%

IR (thin film)

3080(m) 3040(m) 1800(s)(C=O) 1790(s) C=O 1735(w)
1600(s) 1580(m) 1500(m) 1450(s) 1400(w)
1320(w) 1250(w) 1200(s) 1280(m) 1075(w)
1030(w) 1000(w) 870(s) 780(m) cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
7.65	Multiplet	Phenyl	10 protons
4.10	Singlet	Methine	2 protons

Mass spectrum showed a mass ion at 226 m/e.

The product (1) decomposed after a few hours. The melting point of the decomposition product was 70°. A mass spectrum of the decomposition product showed a molecular ion peak at 226 mass units.

The infrared spectrum of decomposition product is :

IR (KBr disc)

1700(s)C=O 1500(m) 1450(m) 1410(s) 1380(s) 1340(m)
1240(s) 760(s) 700(s) cm^{-1}

Fraction (2)

Fraction (2) was identified dibenzyl ketone.

b.p. = 70-90°/0.05mm/Hg
m.p. = 48-52° Yield 40%

IR (KBr disc)

3300-2850(b) 1700(s)(CO) 1600(m) 1580(m)
1500(m) 1450(s) 1420(s) 1330(s)
1290(s) 1180(m) 1130(m) 1070(m)
1030(m) 930(s) 810(m) 710(s) cm^{-1}

NMR (CCl_4) 60MHz

δ	multiplicity	groups	integrals
7.25	Singlet	Phenyl	5 protons
3.60	Singlet	Methylene	2 protons

2 - f : Reactions of dibromoketones.

2 - f - 1: The reaction of 1,3-dibromo-3-methyl-1-phenylbutan-2-one with sodium hydrosulfide.

A solution of sodium (2.3g,0.1 mole) in methanol (50 ml) was saturated with hydrogen sulfide at (10-15°). 1,3-Dibromo-3-methyl-1-phenylbutan-2-one was added dropwise with stirring with the continuous passage of hydrogen sulfide. During the reaction the temperature was kept below 20°. The reaction mixture was left at room temperature under a hydrogen sulfide atmosphere overnight, then poured into water (200 ml) and extracted with diethyl ether. After drying the ethereal solution over anhydrous sodium sulfate, the solvent was removed using a rotary evaporator. The resulting yellow liquid was distilled to give the dithiol and a dimercapto-tetraketone, the structure is discussed on page 148.

Fraction (1)

b.p. - 82-88°/0.05mm/Hg Yield = 45%

IR (thin film)

3100-2840 (m, w) 2560 (w)(S-H) 1715 (s) (C=O)

1600 (m) 1500 (s) 1450 (m) 1370 (m) cm^{-1}

NMR ($CDCl_3$) 60 MHz

δ	multiplicity	groups	integrals
1.20	Singlet	Methyl	6 protons
3.15	Singlet	Thiol	2 protons
3.80	Singlet	Methine	1 proton
7.20	Singlet	Phenyl	5 protons

The mass spectrum of 1,3-dimercapto-3-methyl-1-phenylbutan-2-one did not give the mass molecular ion 226 as expected but showed ions at $\frac{m}{e}$ 222, 221, 210, (Table 7).

Fraction(2)

b.p. = 90-98°/0.05mm/Hg

IR (thin film)

3060-2820(s,m) 2560(w)S-H 1715(s)(C=O) 1600(m)
1480(m) 1450(m) 1360(m) cm^{-1}

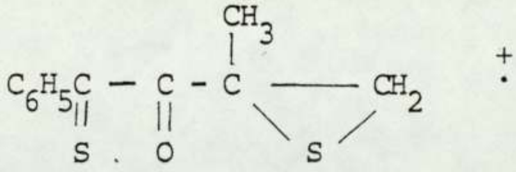
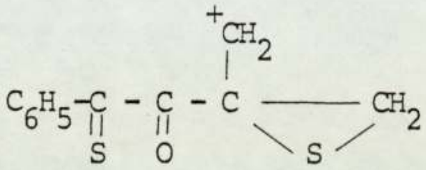
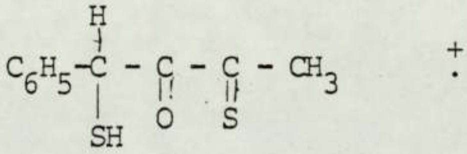
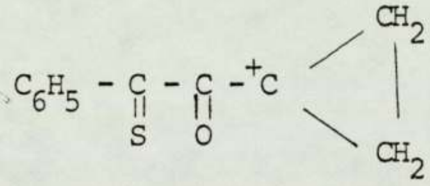
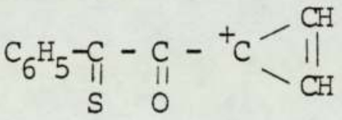
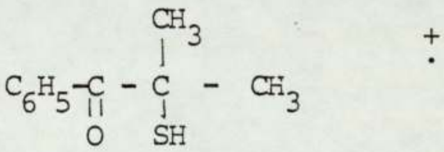
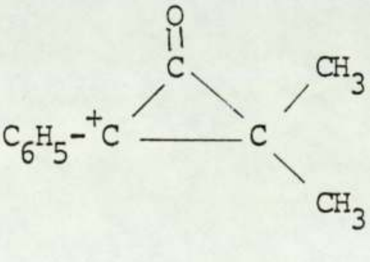
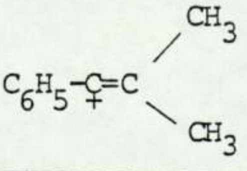
NMR (CCl_4) 30 MHz

δ	multiplicity	groups
1.30	Singlet	Methyl
1.55	Singlet	Methyl
3.20	Singlet	Thiol
3.90	Singlet	Methine
4.00	Singlet	Methine
7.25	Singlet	Phenyl

The mass spectrum gave a parent ion at $\frac{m}{e}$ 576 .

(Table 7)

Mass spectrum of 1,3-dimercapto-3-methyl-1-phenylbutan-2-one

m/e	Fragments
222	
221	
210	
189	
187	
180	
159	
131	

2 - f -2: The reaction of 1,3-dibromo-3-methyl-1-phenylbutan-2-one with sodium sulfide.

Sodium sulfide nonahydrate (25.1g, 0.1 mole) was dissolved in water (250 ml). 1,3-Dibromo-3-methyl-1-phenylbutan-2-one (32g, 0.1 mole) in ethanol (200 ml) was slowly added to the sodium sulfide solution. The reaction mixture was then stirred for three hours at room temperature. The organic layer was extracted with methylene chloride. After drying the combined extracts over anhydrous sodium sulfate, the solvent was removed using a rotary evaporator. Diethyl ether was added to the resulting thick oil. The solid was filtered off and the liquid was distilled after removing the diethyl ether.

Fraction 1 Solid

m.p. = higher than 200°

IR (KBr disc)

3080--3000 (w) 2960 (m) 1700 (s) (C=O) 1500 (m)
1450 (s) 1300 (m) 1140 (w) 1080 (m) 1050 (s)
840 (m) 750 (s) 700 (s) cm^{-1}

The mass spectrum showed mass ion peaks at m/e 351, 317, 281, 235, 224, 191, 178, 160, 162, 164, 153, 154.
The structure of fraction 1 was not identified.

The liquid was distilled to give two fractions -

Fraction 1 b.p. = 92-98°/0.05mm/Hg

Fraction 1 was identified as a mixture of benzyl isopropyl ketone and probably 3-bromo-3-methyl-1-phenylbutan-2-one.

IR (thin film)

3500(b.m) 3100-2860(s) 1720(s)(C=O)

1600(s) 1450(s) 970(m) cm^{-1}

The mass spectrum of fraction 1 showed mass ion at $\frac{m}{e}$ 162.

NMR ($CDCl_3$) 30 MHz

δ	multiplicity	groups
1-1.1	Doublet$^{(K)}$	Methyl$^{(K)}$
1.3	Singlet$^{(X)}$	Methyl$^{(X)}$
2.8	Septet$^{(K)}$	Methine$^{(K)}$
3.7	Singlet$^{(K)}$	Methylene$^{(K)}$
3.9	Singlet$^{(X)}$	Methylene$^{(X)}$
7.3	Singlet$^{(X)(K)}$	Phenyl$^{(K)(X)}$

K = benzyl isopropyl ketone

X = might be 3-bromo-3-methyl-1-phenylbutan-2-one.

<u>Fraction (2)</u>

b.p. = 100-123°/0.05mm/Hg

Fraction (2) was identified as a mixture of 3-bromo-3-methyl-1-phenylbutan-2-one and probably <u>3,3-dimethyl-5-phenyl-1,2-dithiolan-4-one</u>.

IR (thin film)

3050-2900(M,W)(C-H)

1725(s)(C=O) 1600(w) 1490(m) 1450(m) cm^{-1}

NMR $(CDCl_3)$, 60 MHz

δ	Multiplicity	Groups
1.3	Singlet	Methyl (BK)
1.5	Singlet	Methyl (D)
1.6	Singlet	Methyl (D)
3.9	Singlet	Methylene (BK)
4.7	Singlet	Methine (D)
7.1	Singlet	Phenyl (BK)
7.2	Singlet	Phenyl (D)

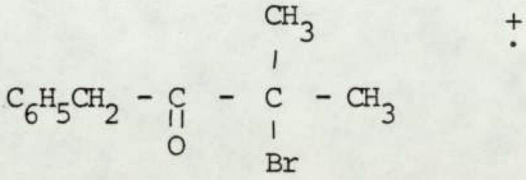
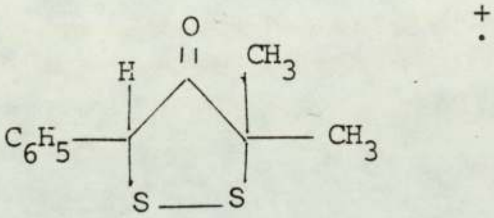
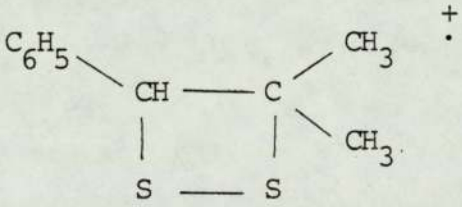
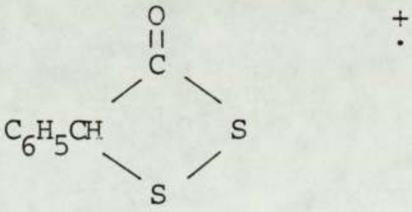
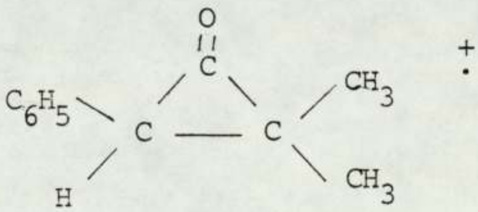
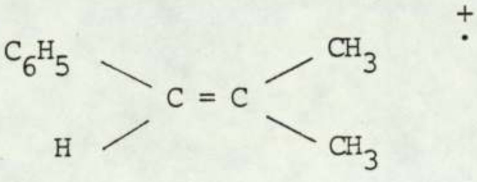
D = 3,3-dimethyl-5-phenyl-1,2-dithiolan-4-one

BK = 3-bromo-3-methyl-1-phenylbutan-2-one

The mass spectrum of fraction 2 showed ions at m/e 224 and 240, 242 respectively due to D and BK (Table 8).

(Table 8)

Mass spectrum of 3,3-dimethyl-5-phenyl-1,2-dithiolan-4-one

m/e	Fragments
240,242	 $C_6H_5CH_2-C(=O)-C(CH_3)(Br)-CH_3^{+\cdot}$
224	
196	
182	
160	
132	

2 - f -:3: The reaction of 1,3-dibromo-3-methylbutan-2-one with sodium sulfide(44).

Sodium sulfide nonahydrate (109.7g, 0.457 mole) was mixed in water (250 ml) with ethyleneglycol (100 ml) and diethyleneglycol dibutylether (150 ml) at 80°. 1,3-Dibromo-3-methylbutan-2-one (110g, 0.451 mole) was added dropwise to the mixture under nitrogen gas. The reaction mixture was stirred at 80° for two hours. The mixture was cooled and the organic layer was extracted with ether. After drying the ethereal phase over anhydrous sodium sulfate , the solvent was removed using a rotary evaporator. The resulting liquid was distilled and two fractions were obtained.

Fraction (1)

b.p. = 70 - 125°/22mm/Hg

Lit. b.p. = 50-75°/25mm/Hg(44)

IR (thin film)

1760(m) (C=O) 1710(s)(C=O) 1450(s) 1350(s) cm^{-1}

Fraction 1 was identified as a mixture of 2,2-dimethylthietan-3-one and 3,3-dimethyl-1,2-dithiolan-4-one in low yield 6%.

Fraction 2: was identified as a 3,3-dimethyl-1,2-dithiolan-4-one.

b.p. - 120-130°/22mm/Hg

IR (thin film)

1715(s)(C=O) 1450(s) 1360(m) 1100(s) cm^{-1}

NMR (CCl$_4$) 30 MHz

δ	multiplicity	groups
3.6	Singlet	Methylene
1.45	Singlet	Methyl

CHAPTER 3

PREPARATION OF SULFENYL CHLORIDES AND THE REACTIONS OF SULFINYL CHLORIDES

Page

CHAPTER 3

CHAPTER THREE

3: Preparation of sulfenyl chlorides and the reactions of sulfinyl chlorides.

3 - a: The reaction of ketones with sulfur dichloride.

3 - a - 1: Benzyl isopropyl ketone.

Sulfur dichloride (1.26 ml, 0.02 mole) in dry carbon tetrachloride (15 ml) was added to benzyl isopropyl ketone (3.24g, 0.02 mole) in dry carbon tetrachloride at 5°. The reaction was run over several days and analyzed at various times using infrared spectrum.

stirred at room for three hours, the product was a mixture of benzyl isopropyl ketone,-3-chlorosulfenyl-3-methyl-1-phenylbutan-2-one and 2-chloro-4,4-dimethyl-2-phenylthietan-3-one.

1780(s)(CO) 1710(s)(CO) 1600(m) 1580(m) 1500(s)
1470(s) 1380(s) 1360(s) 1000(m) 850(m) 800(m)cm^{-1}

δ	multiplicity	groups
1.3 - 0.8	Doublet	Methyl^{K}
1.5	Singlet	Methyl ^{S,T}
3.5	Singlet	Methyl^{T}
7.3	Multiplet	Phenyl^{T,S,K}

K = benzyl isopropyl ketone
S =-3-Chlorosulfenyl-3-methyl-1-phenylbutan-2-one
T = 2-Chloro-4,4-dimethyl-2-phenylthietan-3-one

3 -a - 2: Benzyl isopropyl ketone in the presence of aluminium chloride.

Aluminium chloride (0.5g) was added to benzyl isopropyl ketone (16.2g, 0.1 mole) in dry chloroform (100 ml) at room temperature. Sulfur dichloride (64 ml, 0.1 mole) was then slowly added to the mixture at room temperature. The reaction mixture was refluxed for eight hours. Chloroform was evaporated off and the resulting liquid was distilled.

Three fractions were obtained.

Fraction 1

b.p. = 40-80^{o}/0.12mm/Hg

Fraction 1 was identified as benzyl isopropyl ketone

Fraction 2

b.p. = 80-82^{o}/0.12mm/Hg

IR (thin film)

1720(s)C=O 1610(m) 1500(s) 1470(s) 1390(m) 1050(s)
1000(w) 740(s) cm^{-1}

Fraction 2

Fraction 2 was a mixture of the ketone and 3-chlorosulfenyl-3-methyl-1-phenylbutan-2-one.

NMR (CCl_4) 30 MHz

δ	multiplicity	groups
3.55	Singlet	Methylene
3.85	Singlet	Methylene
3.00 - 1.90	Septet	Methine
1.55	Singlet	Two Methyl
1.10-0.80	Doublet	Two Methyl
7.20	Singlet	Phenyl

Fraction 3

Fraction 3 was a mixture of the ketone, sulfenyl chloride(p. 60) and 2,2-dimethyl-4-phenylthietan-3-one. b.p. = 90-96/0.12mm/Hg

IR (thin film)

3100(w) 3080(m) 2990(s) 2940(m) 1765(m)(C=O) 1720(s)C=O

1670(s) 1605(m) 1500(s) 1460(s) 1070(s) 940(m)

850(w) 750(s) 700(s) cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups
7.20	Multiplet	Phenyl
3.95	Singlet	Methine
3.85	Singlet	Methylene
3.55	Singlet	Methylene
1.80	Singlet	Methyl
1.50	Singlet	Methyl
1·1-08	Singlet	Methyl

3 - a - 3: Benzyl isopropyl ketone in the presence of pyridine.

Pyridine (0.3 ml) was added to benzyl isopropyl ketone (4g, 0.025 mole) in dry chloroform (25 ml) at room temperature.

Sulfur dichloride (1.7 ml), 0.025 mole) was slowly added to this solution and the mixture was refluxed for six hours. Chloroform was evaporated off to give 3-chlorosulfenyl-3-methyl-1-phenylbutan-2-one.

The sulfenyl chloride decomposed under distillation.

IR (thin film)

3100-2850(s) 1700(s)(C=O) 1600(m) 1490(s) 1450(s) 1040(s) 730(s) 690(s) cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.40	Singlet	Methyl	6 protons
3.85	Singlet	Methylene	2 protons
7.20	Singlet	Phenyl	5 protons

3 - a - 4: Ethyl isopropyl ketone in the presence of pyridine.

Pyridine (0.5 ml) was added to ethyl isopropyl ketone (9.9g, 0.1 mole) in chloroform at room temperature.

Sulfur dichloride (6.6 ml 0.1 mole) was added to this solution at 30 - 38°.

The mixture was then heated for one hour at 34°. The chloroform was evaporated off and the pyridine hydrochloride was then filtered off. The resulting green liquid was a mixture of 2-chloro-2,4,4-trimethylthietan-3-one, ethyl isopropyl ketone and the sulfenyl chloride.

IR (thin film)

1780(m) (CO) 1700(s) (CO) 1450(s) cm^{-1}

3 - b The reactions of sulfinyl chlorides.

3 - b - 1: 3-Chlorosulfinyl-3-methylbutan-2-one with aluminium chloride.

Aluminium chloride (0.4g, 0.003 mole) was added to 3-chlorosulfinyl-3-methylbutan-2-one (5.07g, 0.03 mole).

The reaction mixture was stirred for one hour at 40 - 50° under nitrogen. The resulting thick oil was distilled under vacuum to give a colourless liquid, b.p. = 40-50°/mm/Hg. The colourless liquid was 3-chloro sulfinyl-3-methylbutan-2-one. Yield 80%.

IR (thin film)

2980(m) 2940(m) 1700(s)(CO). 1460(m) 1360(s) 1250(m)

1150(s) (S=O) 1110(s) 960cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.65	Singlet	Methyl	6 protons
2.30	Singlet	Methyl	3 protons

3 - b - 2: 2-Chlorosulfinyl-2-,4-dimethylpentan-3-one with aluminium chloride.

Aluminium chloride (10g, 0.08 mole) was added to 2-chlorosulfinyl-2,4-dimethylpentan-3-one (7g, 0.04 mole) in methylene chloride (35 ml) at room temperature for one day. The mixture was hydrolysed by hydrochloric acid (6N).

The organic layer was extracted with methylene chloride. The methylene chloride was then removed to give 2-chlorosulfinyl-2,4-dimethylpentan-3-one. Yield 73%.

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1-1.25	Doublet	Methyl	6 protons
1.7-1.80	Singlet	Methyl	6 protons
2.4-3.5	Septet	Methine	1 proton

3 - b - 3: 3-Chlorosulfinyl-3-methylbutan-2-one with triethylamine.

Triethylamine (4.6g, 0.032 mole) was slowly added to 3-chlorosulfinyl-3-methylbutan-2-one (5.54g, 0.032 mole) in diethyl ether (30 ml) at 5 - 10°. The reaction mixture was then heated at 30° for three hours. The precipitated triethylamine hydrochloride was filtered off. Diethyl ether was further added to the precipitate.

The solution was heated and the precipitate was filtered off immediately. The ethereal layer was then stirred overnight at room temperature to allow further precipitation of the hydrochloride. The ethereal solution was collected and concentrated to 200 ml. The ethereal solution was kept in the cold (-50°) for two weeks. The yellow solid obtained was collected and recrystallized from carbon tetrachloride and petroleum ether, (40 - 60°) The possible structure of the product was explained in Page 164.

m.p. = 11[illegible]

IR (KBr disc)

2980(m) 2920(w) 2680(w) 1690(s) C=O 1460(w)

1360(m) 1300(w) 1260(w) 1220(w) 1145(s) (S=O)

1070(m) 980(m) 920(m) 870(s) 770(m) cm^{-1}

NMR ($CDCl_3$) 30 MHz

δ	multiplicity	groups	integrals	
1.5	Singlet(b)	Methyl	19	12
2.30	Singlet	Methylene	5	3
7.50	Singlet		1.7	1

An expansion of the peak at δ=1.5 ppm showed two lines.

found

C=55.0 H = 7.7 S = 14.6%

Cal. for $C_{10}H_{16}O_3S$ C=55.8 H = 7.4 S = 14.8%

The mass spectrum at 70 ev gave ions at $\frac{m}{e}$ 298, 266, 234, 223, 191, 124, 56.

Accurate mass spectrum of ions at m/e 298, 266

m/e	calculated molecular weight	given molecular weight	molecular formula	error
266	266.0457	266.04688	?$C_{10}H_{18}O_2S_3$	4.2ppm
298	298.01875	298.01896	?$C_{10}H_{18}O_2S_4$	0.7ppm

The mass spectrum at 15 ev gave ions at $\frac{m}{e}$123, 124, 148, 151, 165, 175, 255.

Hydrolysis of the precipitate, which was insoluble in ether, gave triethylamine. The weight of the resultant triethylamine hydrochloride was (4.3g. 0.03 mole).

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.1	Triplet	Methyl	3 protons
2.5	Quartet	Methylene	2 protons

3 - b - 4: 2-Chlorosulfinyl-2,4-dimethylpentan-3-one with thionyl chloride.

Thionyl chloride (18 ml, 0.25 mole) was slowly added to 2-chlorosulfinyl -2,4-dimethylpentan-3-one (9.8g, 0.05 mole) at room temperature. Pyridine (1 ml) was added to the mixture. The mixture was refluxed at 70 - 85° for four days. The excess of thionyl chloride was evaporated off and on distillation the resultant liquid gave two fractions.

Fraction 1 b.p. = 80-82°/4mm/Hg Yield = 40%

The Fraction 1 was identified as a mixture of fraction 2 and unknown compound.

3500(w) 2985(s) 2930(s) 2860(m) 1750(s) (C=O)
1680(s) 1450(s) 1380(s) 1130(s) 1070(s)
1010(s) 850(s) 780(s) cm^{-1}

NMR (CCl_4) 60 MHz

δ	multiplicity	groups
1.45	Singlet	Methyl
1.65	Singlet	Methyl
1.75	Singlet	Methyl
1.95	Singlet	Methyl

Mass spectrum showed molecular ions at $\frac{m}{e}$ 246, 248, 250, 252 (Table 9).

Fraction 2

b.p. = 84-86°/4mm/Hg

IR was similar to Fraction 1.

NMR (CCl_4) 60 MHz

δ	multiplicity	groups	integrals
1.95	Singlet	Methyl	3
1.80	Singlet	Methyl	3
1.60	Singlet	Methyl	3

Mass spectrum show ions at $\frac{m}{e}$ 246, 248, 250, 252.

The resulting liquid was thought to be <u>4,5,5-trichloro-2,2,4 trimethyl-1-thiacyclopentan-3-one</u>.

Table (9)

Mass spectrum of 4,5,5-trichloro-2,2,4-trimethyl-1-thiacyclopentan -3 - one

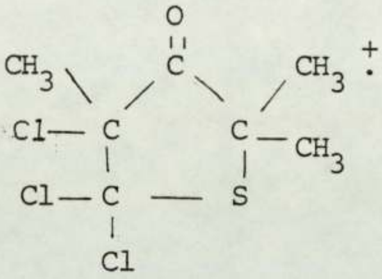
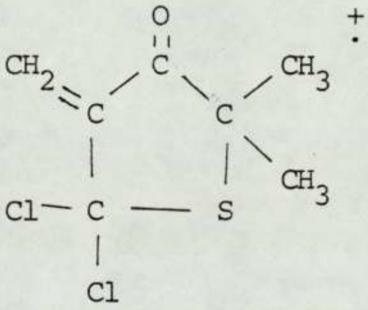
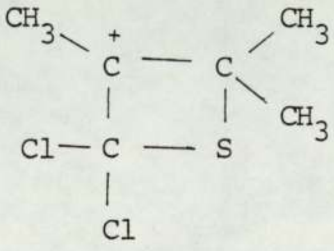
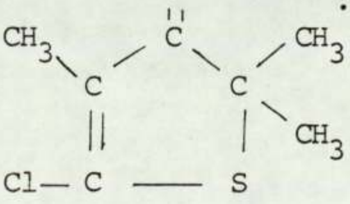
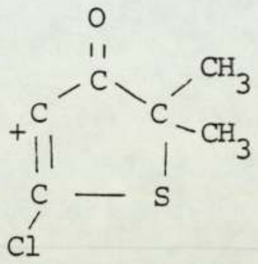
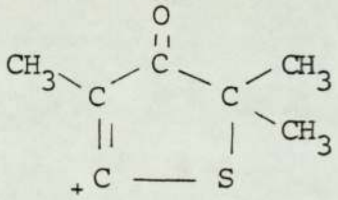
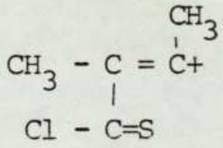
m/e	Fragments	Relative intensity
246, 248, 250, 252		100 : 99 : 33 : 3.8
210, 212, 214		
183, 135, 187		
176, 178		

Table (9) - continued

m/e	Fragments
161, 163	
141	
132	 $CH_3-\underset{Cl-C=S}{\underset{\mid}{C}}=\overset{CH_3}{\overset{\mid}{C}}+$

The existence of three chlorine atoms in the molecule was confirmed by measuring the relative intensity of peaks M, M + 2, M + 4, M + 6.

The accurate mass spectrum of an ion at m/e 246.

m/e	molecular formula	calculated molecular weight	given molecular wt.	error
246	$C_7H_9Cl_3OS$	245.94431	245.94396	1.4ppm

CHAPTER 4

THE REACTIONS OF THIETAN-3-ONES

Page

CHAPTER 4

4 - The reactions of thietan-3-ones

4 - The reactions of thietan-3-ones

4 - a: The reaction of 2-chloro-4,4-dimethyl-2-phenylthietan-3-one with various reagents

4 - a - 1: Piperidine

Dry piperidine (2.1g, 0.025 mole) in dry diethyl ether (15 ml) was added dropwise to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (2.26g, 0.01 mole) in diethyl ether (25 ml) at 20 - 25°. The reaction mixture was stirred at room temperature for two days. The precipitated piperidine hydrochloride was filtered off and washed with dry diethyl ether several times. Piperidine (0.1 ml) was added to the ethereal part and the reaction mixture was then heated at 30° over a water bath for sixty hours. The precipitated piperidine hydrochloride was filtered off and the ether was removed by evaporation under reduced pressure. Methanol (0.5 ml) was added to the resulting thick oil whereupon white crystals were formed. This precipitate was filtered off and recrystallized from methanol to afford 2,2-dimethyl-4-phenyl-4-piperidinothietan-3-one.

m.p. = 50° Yield = 32%.

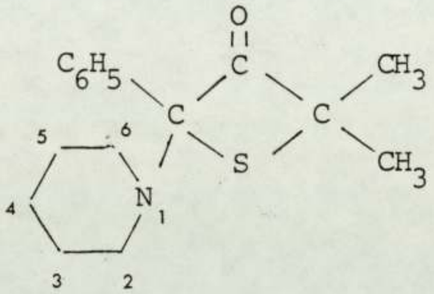
The elemental analysis for molecular formula $C_{16}H_{21}NOS$ is :-

	C	H	N	S
Calculated	69.81	7.63	5.09	11.64 %
Found	69.70	7.80	5.00	12.00 %

IR (KBr disc)

3030 (w) 2940 (s) 2860 (m) 2810 (m) 1760 (s) (C=O)
1590 (w) 1445 (s) 1380 (m) 1360 (m) 1310 (m)
1250 (m) 1230 (m) 1200 (m) 1170 (w) 1110 (w)
1060 (m) 1035 (m) 985 (s) 910 (w) 860 (m)
840 (m) 820 (m) 770 (s) 750 (s) 710 (w)
690 (m) cm^{-1}

NMR (CCl_4) 30MHz

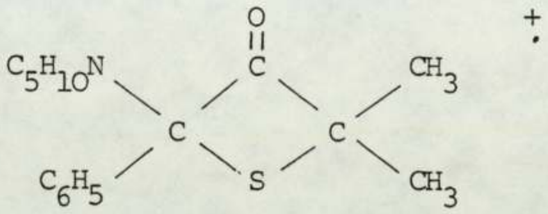
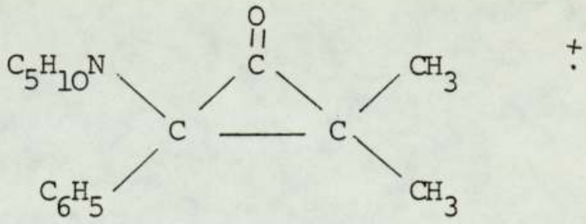
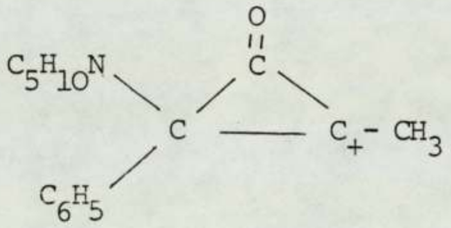
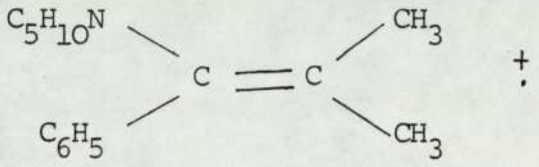
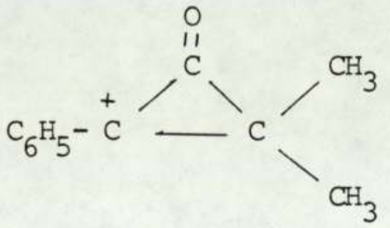


δ	multiplicity	groups	integrals
1.35	S	Methyl	12 protons
1.35-1.80	b.S	Methylene (3,4,5)	
1.60	S	Methyl	
2.50	b.S	Methylene (2,6)	4 protons
7.35-7.70	m	Phenyl	5 protons

The mass spectrum of 2,2-dimethyl-4-phenyl-4-piperidinothietan-3-one gave a molecular ion peak at $\frac{m}{e}$ 275 (Table 10).

(Table 10)

Mass spectrum of 2,2-dimethyl-4-phenyl-4-piperidino thietan-3-one

m/e	Fragments
275	
243	
228	
215	
198	$C_5H_{10}N - C - C{\equiv}C - CH_3$ $^{+\cdot}$
158	
117, 84	$C_6H_5 - \underset{+}{C} = C = O$ $C_5H_{10}N^{+\cdot}$

Accurate mass spectrum of 2,2-dimethyl-4-piperidino-4-phenylthietan-3-one of an ion at m/e 275.

m/e	molecular formula	given molecular weight	calculated molecular weight	error
275	$C_{16}H_{21}NOS$	275.13438	275.13416	0.7ppm

4 - a - 2: <u>Morpholine</u>

Morpholine (2g, 0.023 mole) in dry diethyl ether (10 ml) was slowly added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (2.26g, 0.01 mole) in diethyl ether (25 ml) at room temperature. This reaction mixture was stirred for one day. The precipitated morpholine hydrochloride was filtered off. The ethereal layer was collected and the ether was evaporated off. The resulting solid was recrystallized from methanol to give <u>2,2-dimethyl-4-morpholino-4-phenylthietan-3-one</u>.

m.p. = 127^{o} Yield = 95%

<u>Elemental analysis</u> of $C_{16}H_{21}NOS$

	C	H	N	S
Calculated	64.98	6.86	5.05	11·50
Found	65.10	7.20	5.00	11.80

IR (KBr disc)

675 (w) 700 (m) 725 (m) 760 (s) 800 (s)
830 (w) 860 (w) 875 (s) 925 (s) 965 (w)
990 (w) 1010 (m) 1065 (w) 1080 (vw) 1112 (s)
1150 (vw) 1160 (w) 1190 (m) 1360 (m) 1375 (m)
1390 (vw) 1440 (s) 1485 (m) 1575 (w) 1590 (vw)
1755 (s)(C O) 2820 (m) 2826 (m) 2900 (vw) 2962 (m)
3060 (w) cm^{-1}

NMR (CCl_4) (30 MHz)

δ	multiplicity	integrals	groups
1.3	Singlet	3 protons	$-CH_3$
1.5	Singlet	3 protons	$-CH_3$
2.3	Triplet	4 protons	$-CH_2-N-CH_2-$
3.6	Triplet	4 protons	$-CH_2-O-CH_2-$
7.3 -7.9	Multiplet	5 protons	C_6H_5

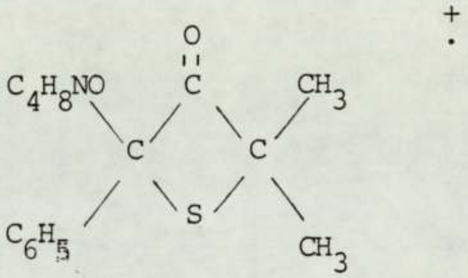
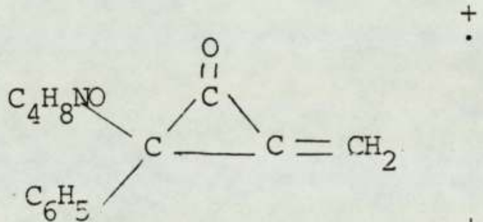
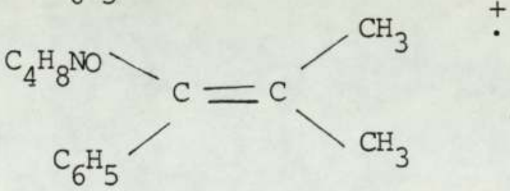
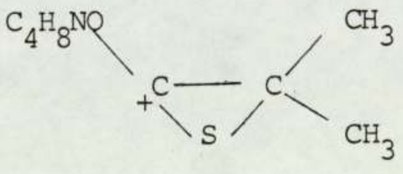
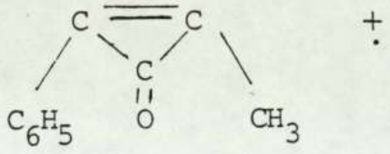
Accurate mass spectrum of 2,2-dimethyl-4-morpholino-4-phenylthietan-3-one of an ion at m/e 277.

m/e	molecular formula	given molecular weight	calculated molecular wt.	error
277	$C_{15}H_{19}NO_2S$	277.11364	277.11398	1.2ppm

The e.s.r. spectrum of the reaction mixture was taken in the presence of a spin trap (nitrone). The e.s.r. spectrum did not show the presence of a radical.

Table (11)

Mass spectrum of 2,2-dimethyl-4-morpholino-4-phenylthietan-3-one.

m/e	Fragments
277	
229	
217	
172	
144	

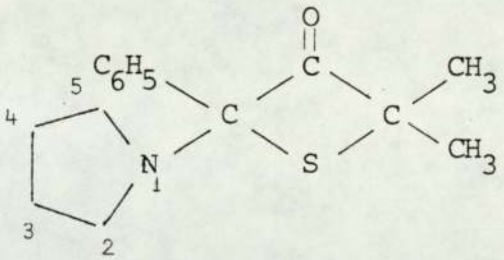
4 - a - 3: Pyrrolidine

Pyrrolidine (15.4g, 0.22 mole) in diethyl ether (30 ml) was added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (22.6g, 0.1 mole) in dry diethyl ether (20 ml) at 0°. The reaction mixture was stirred at room temperature for three days. Pyrrolidine hydrochloride was filtered off. The ether was removed using a rotary evaporator and the resulting red liquid was then distilled under reduced pressure to give 2,2-dimethyl-4-phenyl -4-pyrrolidinothietan-3-one.
b.p. = 90-100°/0.01mm/Hg. Yield = 50%.

The mass spectroscopic data is given in Table (12).

IR (KBr disc)

3080(w) 3040(w) 2980(s) 2940(m) 2880(m)
1760(s)(C=O) 1730(vw) 1630(m) 1600(w) 1500(m)
1450(w) 1380(w) 1365(w) 1350(w) 1265(m)
1170(w) 1120(m) 1070(m) 1020(m) 750(w)
700(m) 720(m) cm^{-1}



NMR (CCl_4) 30 MHZ

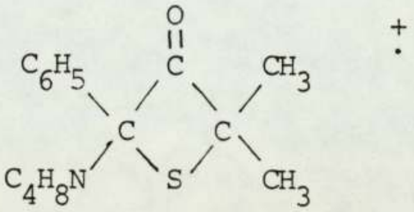
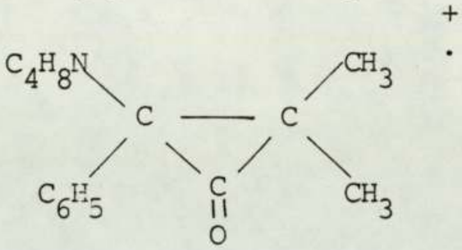
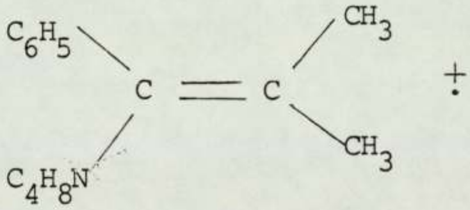
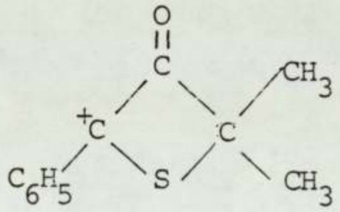
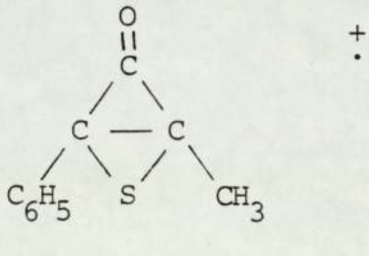
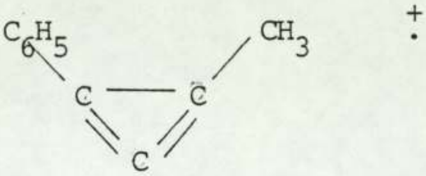
δ	multiplicity	groups	integrals
1.35	Singlet	Methyl	3 protons
1.55	Singlet	Methyl	3 protons
2.60	Multiplet	Methylene (2,5)	4 protons
1.20 - 1.90	2.broad Singlet	Two Methyl and Methylene (3,4)	10 protons
7.20	Multiplet	Phenyl	5 protons

Accurate mass spectrum of 2,2-dimethyl-4-phenyl-4-pyrrolidinothietan-3-one of an ion at m/e 261.

m/e	molecular formula	calculated molecular weight	given molecular wt.	error
261	$C_{15}H_{19}NOS$	261.11837	261.11873	1.3ppm

Table (12)

Mass spectrum of 2,2-dimethyl-4-phenyl-4-pyrrolidinothietan-3-one.

m/e	Fragments
261	
229	
201	
191	
176	
126	

4 - a - 4: Hydrazine Hydrate

Hydrazine hydrate (2.21g, 0.04 mole) was added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (4.25g, 0.02 mole) in dry diethyl ether (70 ml). The reaction mixture was stirred overnight at room temperature and diethyl ether was added to the resulting mixture. The ethereal layer was separated from the aqueous layer, diethyl ether was then removed and the solid product was recrystallized from benzene to give 3-(1-mercapto-1-methylethyl)-4-phenyl-Δ^4-1,2-diazetin-3-ol.

m.p. = 120 - 128° Yield = 67%

Elemental analysis of $C_{11}H_{14}N_2OS$

	C	H	N	S
Found	59.61	6.20	12.60	14.10 %
Calculated	59.46	6.30	12.60	14.41 %

IR (KBr disc)

3420(s) 3285(m) 2960(w) 2900(w) 2850(vw)
2575(w)(S–H) 1645(s) 1600(m) 1590(m) 1550(s)
1480(w) 1440(w) 1380(m) 1360(w) 1325(s)
1235(m) 1190(w) 1130(w) cm^{-1}

IR ($CHCl_3$)

3465(s) 3305(m) 3200(w) 2980(w) 2910(w)
2860(w) 2580(w) 1660(s) 1605(m) 1565(s)
1490(m) .... cm^{-1}

NMR($CDCl_3$) 60 MHz

δ	multiplicity	groups	integrals
1.75	Singlet	Methyl	6 protons
3.05	Singlet	Thiol	1 proton
6.15	Singlet	Amine	2 protons
7.35	Multiplet	Phenyl	5 protons

The nuclear magnetic resonance spectrum of the product was taken at various concentrations in $CDCl_3$

$W/_V$	Conc. of Solution	δ of NH_2
0.053/0.5	10.6%	6.05
0.053/1	5.3%	5.85
0.053/1.5	3.5%	5.75

W = The weight of the resulting compound of the reaction (4-a-4)

V = The volume of $CDCl_3$

u.v. (cyclohexane)

(A) - 0.0111g of the resulting compound of the reaction (4-a-4) was dissolved in cyclohexane (25 ml). 0.3 ml of (A) was dissolved in cyclohexane (10 ml).

$C g/lit = 0.3 \times 0.0111 \times 1000/_{10 \times 25} = 0.01332$

$C\ mole/lit = 0.01332/_{222} = 6 \times 10^{-5}$

The u.v. spectrum of (7-a-4) shows-

λ = 270nm   A = 0.514   L = 1 cm

A = ELC   E = 865 molar extinction coefficient.

NMR ($CDCl_3$ + shift reagent) 60 MHz

δ	multiplicity	groups
7.35	Multiplet	Phenyl
6.10	Singlet (b)	NH, OH?
3.00	Singlet	Thiol
1.75	Singlet	Methyl
1.1 - 1.20	Two Singlet	Shift reagent

NMR ($CDCl_3$ + D_2O + Shift reagent) 60 MHz

δ	multiplicity	groups
7.35	Multiplet	Phenyl
6.10	Singlet (b)	OH?
4.65	Singlet	Thiol?
3.75	Triplet	NH
1.75	Singlet	Methyl
1.10-1.20	Two singlet	Shift reagent

Figures 6, 7 and 8 show the ^{13}C, NON and NOE nuclear magnetic resonance spectrum of (4-a-4).

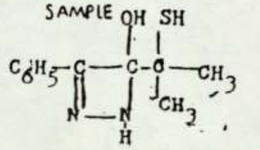
The mass spectrum of (4-a-4) showed a molecular ion peak at 222 mass units (Table 13, 14, 15).

Accurate mass spectrum of (4-a-4) of an ion at m/e 222.

m/e	molecular formula	given molecular weight	calculated molecular wt.	error
222	$C_{11}H_{14}N_2OS$	222.08301	222.08268	1.4ppm

90Q

SAMPLE



SOLVENT $CDCl_3$
CONCENTRATION
REFERENCE TMS
TEMPERATURE R.T

NUCLEUS ^{13}C
OBS 22.5 MHZ
LOCK
IRR
OFFSET
OBS
IRR
PULSE ✓ SINGLE
WIDTH
INTERVAL 1
REPETITION 1

DATA POINTS 8000
WINDOW
NO

SPECTRAL WIDTH 10000
RF GAIN
AMPLITUDE 20

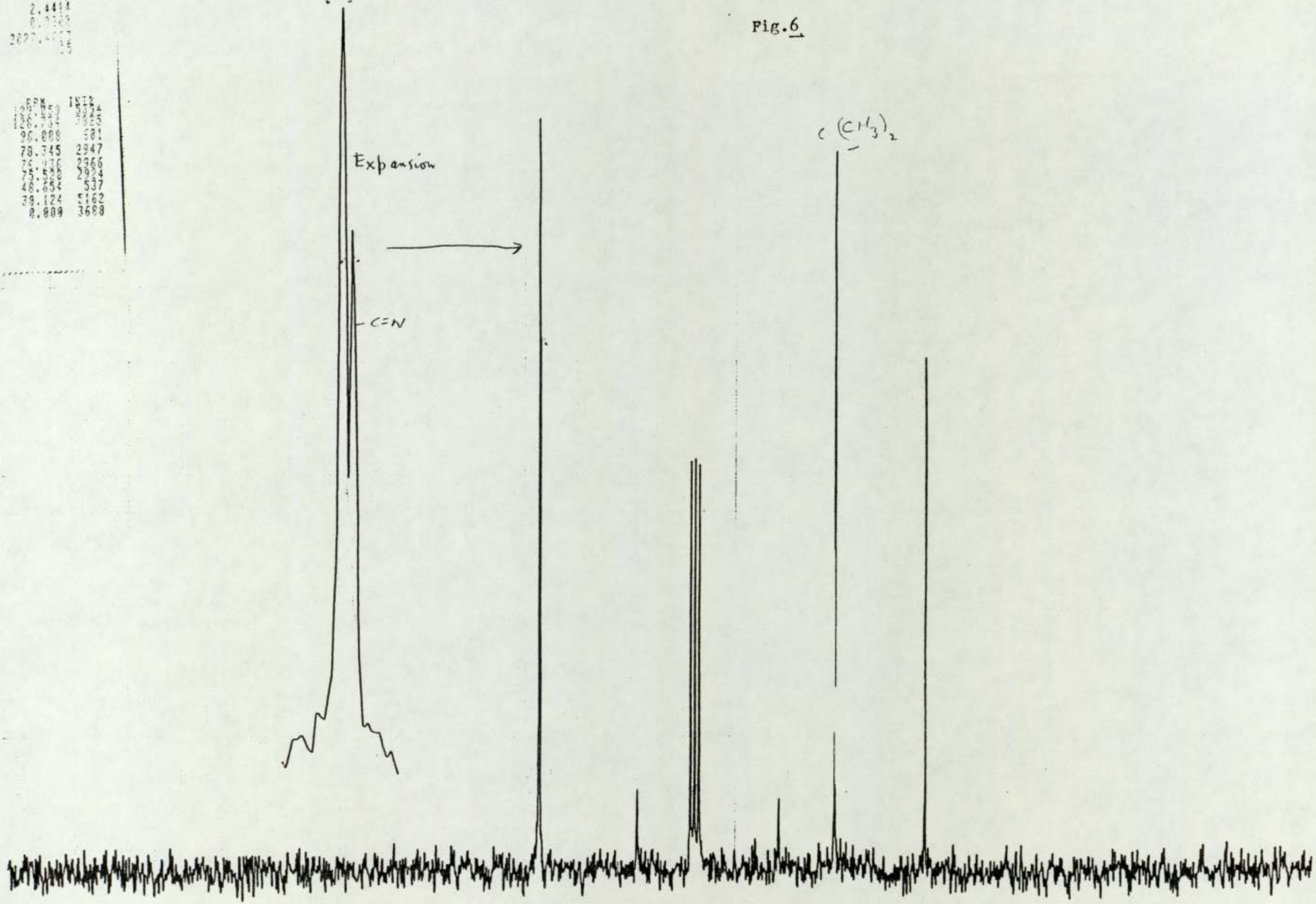
DECOUPLING COM
CW ✓ NOISE
HOMO
POWER

RF LEVEL high 6

AMPLITUDE 25

DATE

Fig.6



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EF            0.[illegible]
[illegible]   2027.[illegible]
AIR           [illegible]

  FREQ(HZ)      PPM        INT
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  2986.35       126.[illegible]  3585
  2163.40       96.009     581
  1765.13       78.345     2947
  1733.79       76.[illegible]  2366
  1701.66       75.520     2924
  1056.19       46.854     537
   678.71       30.124     5162
     0.00        0.000     3688
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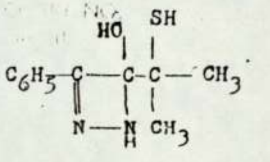
FX 90Q



$C_6H_5-C(=N-NH)-C(OH)(SH)-C(CH_3)_2$

SOLVENT CDCl$_3$
CONCENTRATION
REFERENCE TMS
TEMPERATURE R.T.

NUCLEUS ^{13}C
OBS 22.5 MHZ
LOCK ✓
IRR
OFFSET
OBS KHZ
IRR KHZ
PULSE ☑ SINGLE ☐ MULTI
WIDTH μSEC
INTERVAL SEC
REPETITION SEC

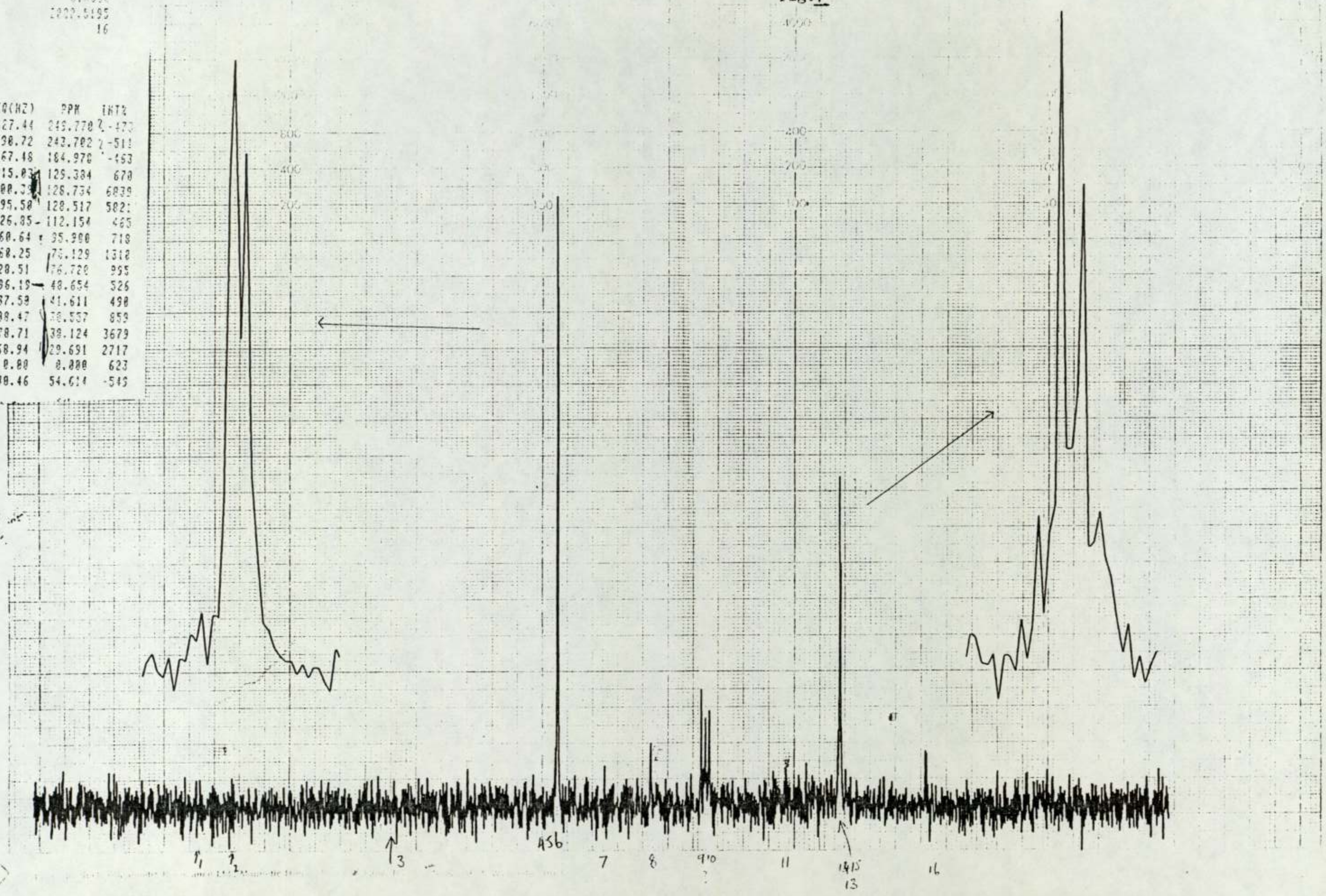
DATA POINTS 8000
WINDOW
NO OF PULSES

SPECTRAL WIDTH 10000
RF GAIN
AMPLITUDE 20

DECOUPLING: NONE
☐ CW ☐ NOISE
☐ HOMO ☐ HETERO
POWER
LOCK
RF LEVEL high 6
RF GAIN
AMPLITUDE 25
DATE 9/11/81
OPERATOR
REMARKS

JEOL

Fig.7



```
                17
   [illegible]
   [illegible]
         2000.5195
                16

FREQ(HZ)    PPM    INT%
 5627.44  249.770  -472
 5498.72  243.702  -511
 4167.48  184.970  -453
 2915.03  129.384   670
 2900.39  128.734  6839
 2895.58  128.517  5821
 2526.85  112.154   465
 2160.64   95.990   718
 1768.25   78.129  1318
 1728.51   76.720   955
 1096.19   48.654   526
  937.59   41.611   490
  698.47   30.557   859
  678.71   30.124  3679
  668.94   29.691  2717
    0.00    0.000   623
-1230.46   54.614  -545
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TOTAL            15
[illegible]      2.4414
REF              0.0000
OSFZ          2877.6367
GAIN             17

 0 FREQ(HZ)     PPM   INT%
 1  2978.51  132.201  2689
 2  2971.19  131.877  2443
 3  2817.39  125.958  2864
 4  2810.85  124.724  2639
 5  2153.32   95.575  4589
 6  1755.37   77.912 10614
 7  1740.72   77.262  1389
 8  1723.63   76.583 10765
 9  1708.98   75.853  1325
10  1691.99   75.094 10238
11   734.86   32.616  1278
12   605.46   26.873  1443
13   476.87   21.130   581
14    48.82    2.166   645
15   -70.88    3.142   682
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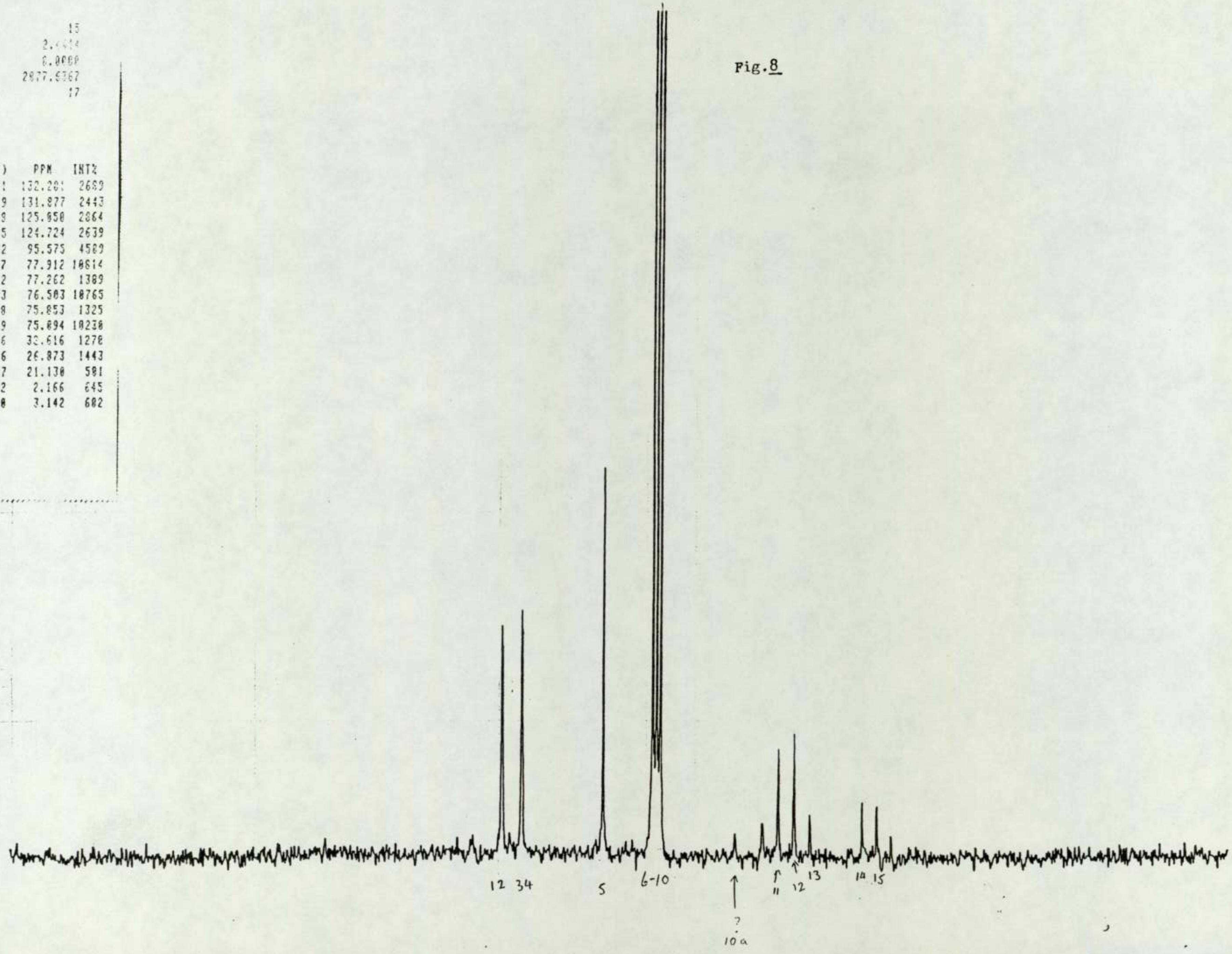
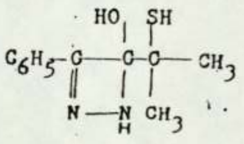
Fig.8





$C_6H_5-C(=N-NH)-C(OH)-C(SH)(CH_3)-CH_3$

SOLVENT $CDCl_3$

REFERENCE TMS
TEMPERATURE R.T.

NUCLEUS ^{13}C
OBS
LOCK ✓22.5
IRR 89.55
OFFSET
OBS 33.0
IRR 54.5
PULSE / SINGLE
WIDTH
INTERVAL 1
REPETITION 1

DATA POINTS 8000
WINDOW —
NO OF PULSES 50000

SPECTRAL WIDTH 10000
RF GAIN
AMPLITUDE

DECOUPLING NON
CW NOISE

RF LEVEL high 6
~~26~~ 5.5
26

5/11/81.

Table (13):

Mass spectrum of
3-(1-Mercapto-1-methylethyl)-4-phenyl-Δ^4-1,2-diazetin-3-ol.

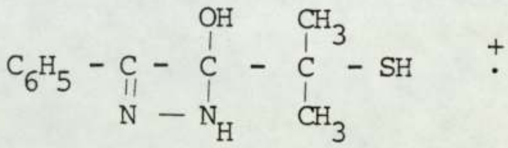
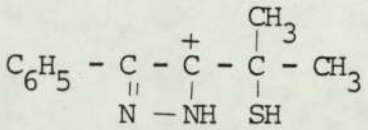
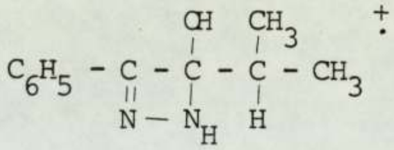
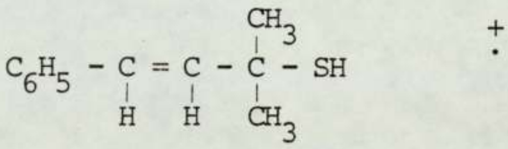
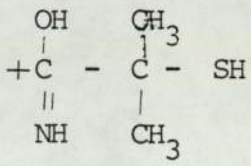
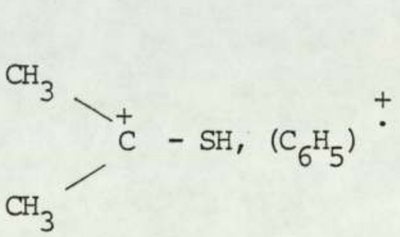
m/e	Fragments
222	 $[C_6H_5 - C(=N - NH) - C(OH) - C(CH_3)_2 - SH]^{+\cdot}$
205	 $C_6H_5 - C(=N - NH) - \overset{+}{C} - C(CH_3)(SH) - CH_3$
190	 $[C_6H_5 - C(=N - NH) - C(OH) - CH(CH_3) - CH_3]^{+\cdot}$
178	 $[C_6H_5 - CH = CH - C(CH_3)_2 - SH]^{+\cdot}$
119	 $+C(OH)(=NH) - C(CH_3)_2 - SH$
104	$C_6H_5 - \overset{+}{C}{=}NH$
103	$[C_6H_5 - C\equiv N]^{+\cdot}$
75, 77	 $(CH_3)_2\overset{+}{C} - SH,\ (C_6H_5)^{+\cdot}$

Table (14)

Mass spectrum of 2-hydrazono-2-mercapto-3-methyl-1-phenylbutan-1-one.

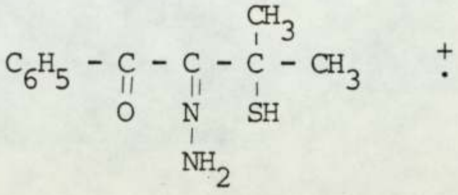
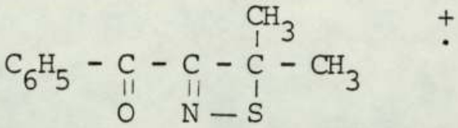
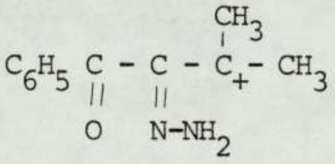
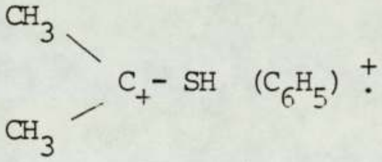
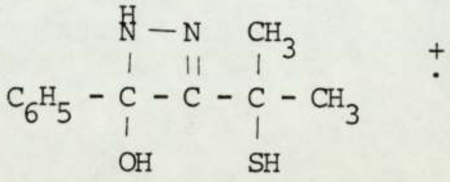
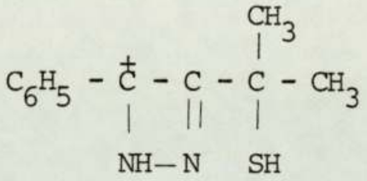
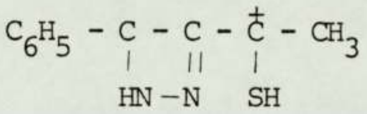
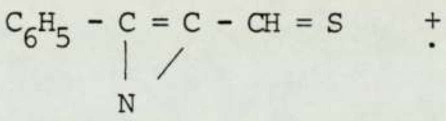
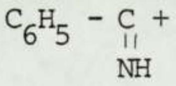
m/e	Fragments
222	 $C_6H_5-C(=O)-C(=N-NH_2)-C(CH_3)(SH)-CH_3\ ^{+\cdot}$
205	 $C_6H_5-C(=O)-C(=N-S)-C(CH_3)-CH_3\ ^{+\cdot}$
190	 $C_6H_5\ C(=O)-C(=N-NH_2)-C_{+}(CH_3)-CH_3$
119, 103, 104	?
75, 77	 $(CH_3)_2C_{+}-SH\ \ (C_6H_5)\ ^{+\cdot}$

Table (15):

Mass spectrum of
4-(1-mercapto-1-methylethyl)-3-phenyl-Δ^4-1,2-diazetin-3-ol.

m/e	Fragments
222	 $C_6H_5-\underset{OH}{\overset{\overset{H}{N}}{C}}-\overset{N}{\overset{\|}{C}}-\underset{SH}{\overset{CH_3}{C}}-CH_3 \quad ^{+\cdot}$
205	 $C_6H_5-\underset{NH}{\overset{+}{C}}-\underset{\overset{\|}{N}}{C}-\underset{SH}{\overset{CH_3}{C}}-CH_3$
190	 $C_6H_5-\underset{HN}{C}-\underset{\overset{\|}{N}}{C}-\underset{SH}{\overset{+}{C}}-CH_3$
160	
104	 $C_6H_5-\underset{NH}{\overset{}{C}}\,^{+}$
119	?

Determination of the chemical shift of the amino group (NH_2) in the hydrazono compound.

Preparation of 2-hydrazono-3-methyl-1-phenylbutane.(75)

Hydrazine hydrate (4g, 0.08 mole) was added to barium oxide (15.3g, 0.1 mole) in ethanol (10 ml). Benzyl isopropyl ketone (13g. 0.08 mole) was slowly added to the mixture at ($10 - 15^{o}$). The reaction mixture was then stirred for two days. The organic fraction was extracted with diethyl ether and the diethyl ether was then removed using a rotary evaporator, to give 2-hydrazono-3-methyl-1-phenylbutane.

IR (thin film)

3325(s)	3190(w)	3040(w)	3000(w)	2900(s)
1580(s)(C=N)		1440(s)	1370(m)	1020(s) cm^{-1}

NMR (CCl_4) 60 MHz

δ	multiplicity	groups	integrals
1.oo	Doublet	Methyl	6 protons
3.45	Singlet	Methylene	2 protons
5.05	Singlet	Amine	2 protons
7.2o	Singlet	Phenyl	2 protons

Detection of carbonyl group of (4-a-4).

The compound resulting from reaction (4-a-4) 0.1g was dissolved in ethanol in hydrochloric acid. The mixture was allowed to stand at room temperature overnight. The crystals were filtered off.

m.p. = 180-182°.

NMR ($CDCl_3$) 30 MHz

δ	multiplicity	groups
1.55	Singlet	Methyl
2.35	Singlet	Thiol
7.55	Multiplet	Phenyl

NMR (C_6D_6) 30 MHz

δ	multiplicity	groups
1.55	Singlet	Methyl
2.35	Singlet	Thiol
7.55	Multiplet	Phenyl
8.30	Singlet(b)	Amine

IR (KBr disc)

3500-3000(b) 1700(s) (C=O) 1590(m) 1450(m) cm^{-1}

The reaction of (4-a-4) with 2,4-dinitrophenylhydrazine sulfate .. Brady's(76) method - A stock solution of 2,4-dinitrophenylhydrazine sulfate in methanol was prepared as follows.

2,4-Dinitrophenylhydrazine 2g was treated with concentrated sulfuric acid (4 ml) and methanol (30 ml) was added cautiously with cooling. After warming to effect complete solution, water (10 ml) was added to the solution. The compound resulting from reaction (4-a-4) (0.1g) was dissolved in the minimum amount of the methanol.
The solution was treated with (3-5ml) of stock solution (dinitrophenylhydrazine solution) and the mixture was refluxed for ten minutes. The solution was cooled. The precipitate was filtered off and collected. m.p. = 135-145°d.

IR (KBr disc)

3260(m)	3100-2940(b)	2660(w)	1615(s) (C=N)
1590(w)	1570(w)	1500(s)	1420(s)
1340(s)	1320(m)	1220(w)	1180(w)
1060(s)	1000(s)	920(m)	790(s) cm^{-1}

4 - a - 5: Phenylhydrazine

Phenylhydrazine (.05 mole, 5.45g) in dry diethyl ether was added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (0.025 mole, 5.56g) in dry diethyl ether at 15 - 20° . The reaction mixture was stirred for one week at 30°. The phenylhydrazine hydrochloride was filtered off. The ethereal solution was allowed to stand at room temperature for three weeks and then evaporated to dryness. The product was recrystallized from a mixture of chloroform and methanol to give 4,4,4',4',-tetramethyl-3,3'-dioxo-2,2'-diphenyl-2,2'-bithietanyl. m.p. = 137-139°. Yield = 20%.

Another method used for the purification of the product was chromatography on an alumina column, using 5% benzene in petroleum ether (40 - 60°).

The mass spectrum of the product showed a molecular ion peak at 382 mass units (Table 16).

IR (KBr disc)

3060(w)	2980(m)	2920(m)	2850(w)	1770(s)(C=O).
1490(s)	1440(s)	1360(m)	1380(m)	1330(w)
1235(w)	1135(s)	1060(m)	1030(w)	910(m)
740(s)	700(s) cm^{-1}			

NMR (CCl_4) 60 MHz

δ	multiplicity	groups	integrals
1.30	Singlet	Methyl	6 protons
1.52	Singlet	Methyl	6 protons
7.20	Singlet	Phenyl	10 protons

An e.s.r. spectrum of the reaction mixture was taken using different conditions in the following manner.

Phenylhydrazine (0.02 mole) in diethyl ether was added to 2-chloro-4,4-dimethylthietan-3-one (0.01 mole) in diethyl ether.

The reaction mixture was stirred for one day. The e.s.r. spectrum of the ethereal fraction was run at room temperature, at 0° and in the presence of a spin trap. The detection of a radical was possible using a spin trap. The e.s.r. spectrum of the starting materials, phenylhydrazine and 2-chloro-4,4-dimethyl-2-phenylthietan-3-one, was taken using the same conditions.

Figure 9 shows the e.s.r. spectrum for the reaction mixture

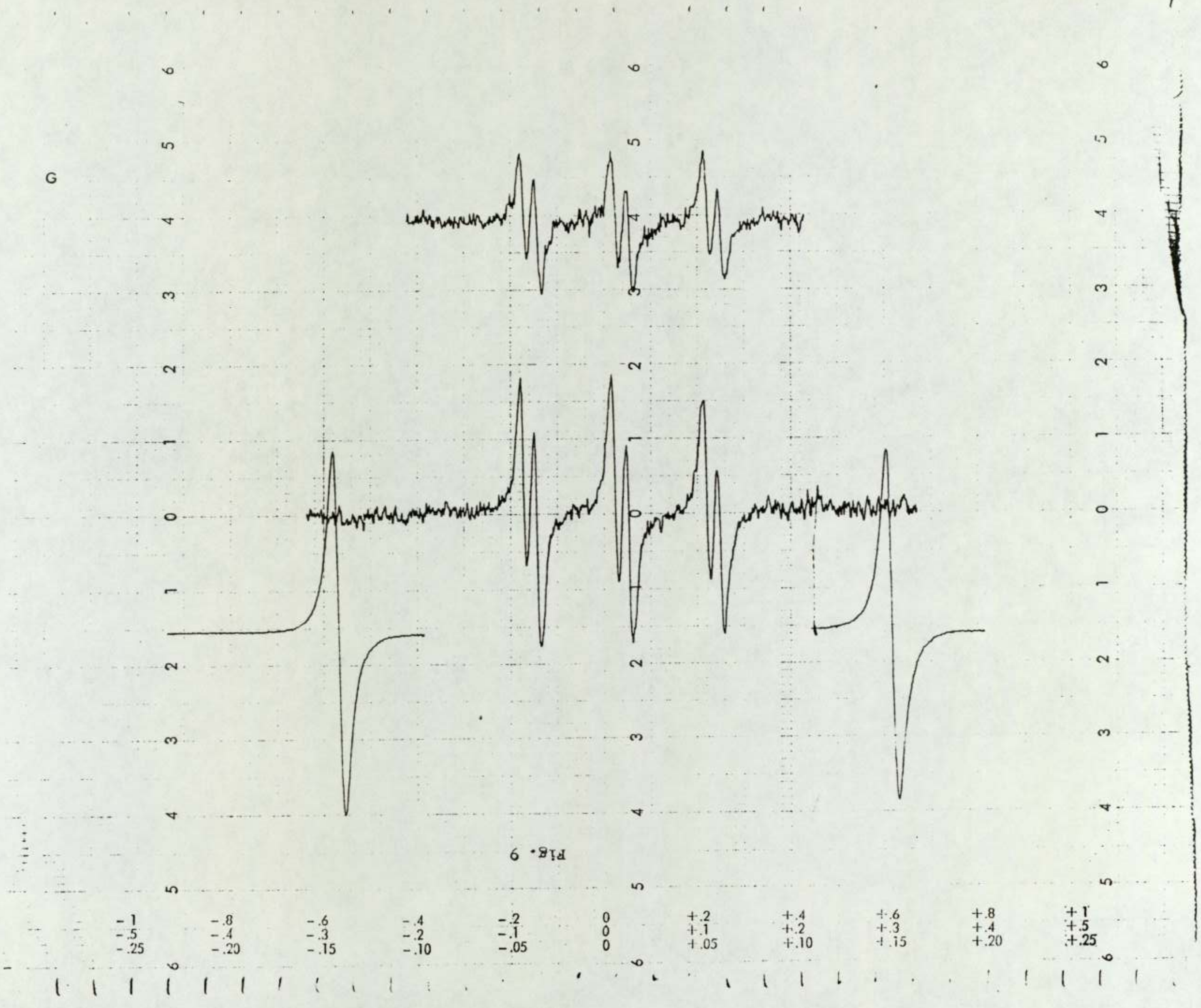

G
6
5
4
3
2
1
0
1
2
3
4
5
6
- 1 - .5 - .25
- .8 - .4 - .20
- .6 - .3 - .15
- .4 - .2 - .10
- .2 - .1 - .05
0 0 0
+ .2 + .1 + .05
+ .4 + .2 + .10
+ .6 + .3 + .15
+ .8 + .4 + .20
+ 1 + .5 + .25

Fig. 9

Table (16)

Mass spectrum of
4,4,4',4'-tetramethyl-3,3'-dioxo-2,2'-diphenyl-2,2'-bithietanyl

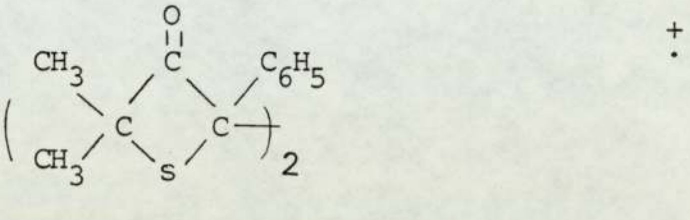
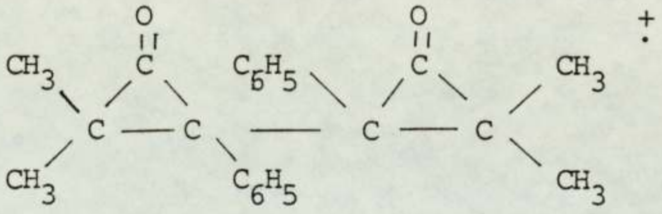
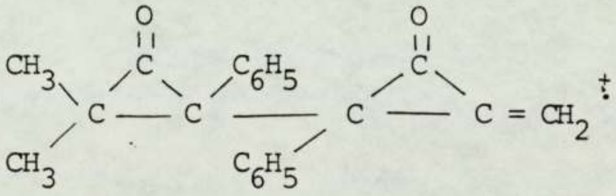
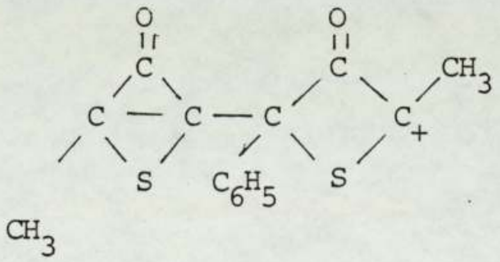
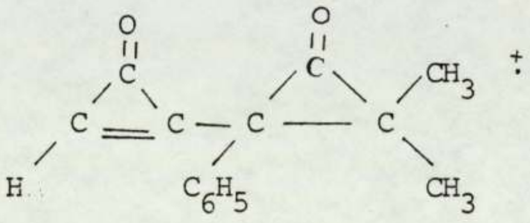
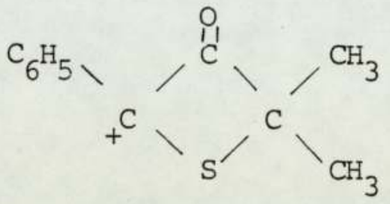
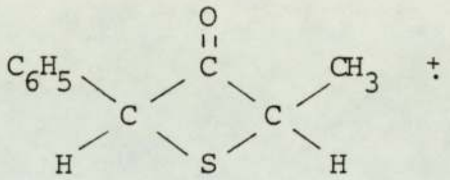
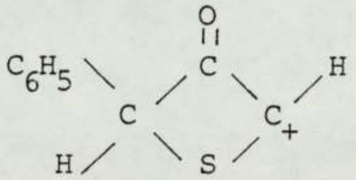
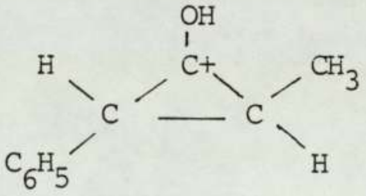
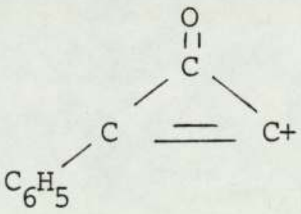
m/e	Fragments
382	
318	
302	
275	
210	

Table (16) continued

m/e	Fragments
191	
178	
163	
147	
129	

4 - a - 6: Methylhydrazine

Methylhydrazine (0.92g, 1.2 ml, 0.02 mole) in dry diethyl ether was slowly added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (2.26g, 0.01 mole) in dry ether (50 ml), at -50°. The precipitated methylhydrazine hydrochloride was immediately filtered off. The ether was evaporated. The products were separated using column chromatography on an alumina (Al_2O_3) column with 5% benzene in petroleum ether (40 - 60°).

Fraction (1)

Fraction 1 was thought to be 2,2-dimethyl-4-methylazo-4-phenylthietan-3-one

IR (thin film)

3060(w) 3020(vw) 2960(m) 2925(s) 2860(w)
1765(s)(C=O) 1600(w) 1480(w) 1445(s) 1360(w) 700(s) cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.2	Singlet	Methyl	3 protons
1.5	Singlet	Methyl	3 protons
1.6	Singlet	Methyl	3 protons
7.3	Multiplet	Phenyl	5 protons

Fraction 2

Fraction 2 was thought to be 3,3,6-trimethyl-1-phenyl-2-thia-5,6-diazabicyclo (2.2.0)hex-4-ene.

IR (thin film)

3300(w,b) 320(w) 2980(m) 2930(s) 2860(w)
1655(s)(C=N) 1550(m) 1450(m) 1480(m) 1380(w)
1100(m) 940(m) cm^{-1}

4 - a - 7: Methanol

Dry methanol (50 ml) was slowly added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (2.26g, 0.1 mole) and dry pyridine (0.3 ml). The reaction mixture was stirred for four days at room temperature. The excess methanol was removed using a rotary evaporator. Dry ether (50 ml) was added to the resulting liquid. Pyridine hydrochloride was filtered off and the ether was then removed. The product was distilled to give 4-methoxy-2,2-dimethyl-4-phenylthietan-3-one.

b.p. = 98 /0.06mm/Hg Yield = 60%.

IR (thin film)

3030(W)	2980(m)	2940(m)	2820(W)	1770(S)(CO)
1680(W)	1500(W)	1450(S)	1370(W)	1385(W)
1190(m)	1100(m)	1060	1030(VW)	980(S)
920(W)	860(m)	830(W)	760(m)	720(W) cm^{-1}

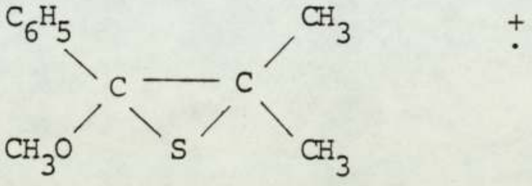
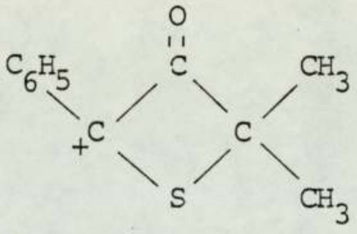
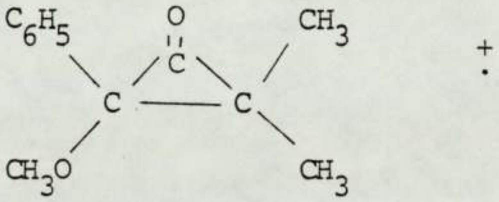
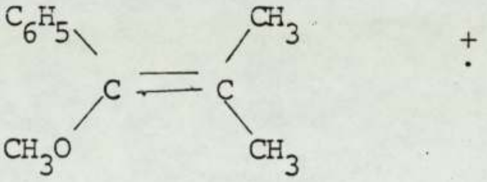
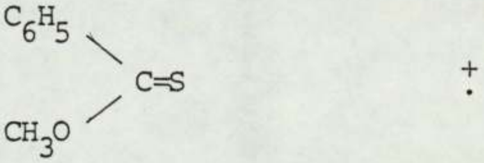
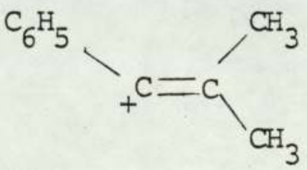
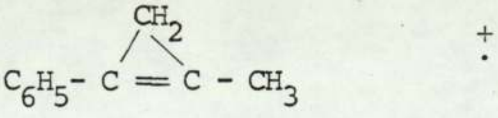
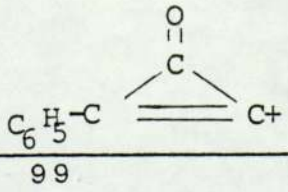
NMR (CCl_4)60 MHz

δ	multiplicity	integrals	groups
1.4o	Singlet	3 protons	Methyl
1.7o	Singlet	3 protons	Methyl
3.4 o	Singlet	3 protons	Methoxy
7.45	Multiplet	5 protons	Phenyl

The mass spectrum of 4-methoxy-2,2-dimethyl-4-phenylthietan-3-one did not give a molecular ion peak at 222 as expected, but showed peaks at $\frac{m}{e}$ 194, 191, 190, (Table 17).

Table (17)

Mass spectrum of 4-methoxy-2,2-dimethyl-4-phenylthietan-3-one.

m/e	Fragments
194	
191	
190	
162	
152	
131	
130	
129	

The accurate mass spectrum of 4-methoxy-2,2-dimethyl-4-phenylthietan-3-one of ions at $^{m}/_{e}$ 194, 190.

m/e	molecular formula	given molecular weight	calculated molecular wt.	error
194	$C_{11}H_{14}OS$	194.07653	194.07615	1.9ppm
190	$C_{12}H_{14}O_2$	190.099373	190.09953	1.00ppm

4- a - 8: Sodium Methoxide.

Sodium methoxide (1g, 0.01 mole) was added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (3.4g, 0.015 mole) at 20°. The reaction mixture was stirred overnight at 30°. Dry diethyl ether was used for the separation of the product from sodium chloride. The ether was removed and the resulting yellow liquid was distilled to give 4-methoxy-2,2-dimethyl-4-phenylthietan-3-one. Yield = 50% b.p. = 88/0.05mm/Hg.

IR (CCl_4)

3000 - 2900(m) 1760(s)(C=O) 1450(s) 1270(s) 1230(s) 1050cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.65	Singlet	Methyl	3 protons
1.45	Singlet	Methyl	3 protons
3.35	Singlet	Methoxy	3 protons
7.3 o	Multiplet	Phenyl	5 protons

4 - a - 9: Benzylmercaptan

Anhydrous pyridine (1.1 ml, 0.01 mole) was dissolved in 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (0.015 ml, 3.398g). Benzylmercaptan (0.015 mole, 2,1g) was added dropwise to the mixture. The temperature of the reaction was controlled between 35-40°. The reaction mixture was stirred for three days at room temperature. Dry diethyl ether (46-60 ml) was added to the resulting solid and the solution was then heated at 40°. The precipitated pyridine hydrochloride was filtered off and the ether was removed using a rotary evaporator. The solid product was recrystallized from petroleum ether (40-60°) to give <u>2-benzylmercapto-4,4-dimethyl-2-phenylthietan-3-one</u>.

m.p. = 50-55°   Yield = 64%

The reaction was carried out under three conditions.

(1) without solvent.
(2) in diethyl ether.
(3) in pyridine.

The third condition was the best, and was subsequently used to isolate the product.

Elemental analysis of $C_{18}H_{18}OS_2$

	C	H	S
Calculated	68.78	5.73	20.38 %
Found	68.20	5.90	20.80 %

IR (thin film)

3080 (vw)	3060 (w)	3020 (m)	2970 (m)	2920 (m)
2850 (w)	1760 (s) (C=O)		1600 (w)	1495 (s)
1450 (s)	1380 (w)	1360 (m)	1240 (w)	1120 (s)
1065 (w)	1030 (w)	960 (w)	800 (w)	750 (s)
700 (s) cm^{-1}				

NMR (CCl_4) 60 MHz

δ	multiplicity	groups	integrals
1.5o	Singlet	Methyl	3 protons
1.75	Singlet	Methyl	3 protons
3.7o- 3.4o	Doublet	Methylene	2 protons
4.1o- 3.8o	Doublet	Methylene	
7.2o	Multiplet	Phenyl	5 Protons

4 - a - 10: Water

Water (25 ml) was added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (0.01 mole, 2.26g). The reaction mixture was stirred at 50° for seven days. The organic layer was extracted with diethyl ether. The ethereal fraction was collected and dried over anhydrous sodium sulfate . The ether was evaporated and the resulting compound was distilled under reduced pressure. The yellow liquid obtained was 3-mercapto-3-methyl-1-phenyl-1,2-butanedione. b.p. = 65 - 67°/0.12mm/Hg. Yield = 81%.

The mass spectrum of 3-mercapto-3-methyl-1-phenyl-1,2-butanedione gave a molecular ion peak at 208 mass units (Table 18).

IR (thin film)

3075(w) 3030(vw) 2980(s) 2940(m) 2860(w)
2565(w)(SH) 1715(s)(C=O) 1675(s)(C=O)
1600(s) 1585(m) 1500(w) 1455(s) 1390(w)
1370(m) 1320(m) 1290(s) 1220(s) 1180(w)
1130(w) 1090(s) 1000(w) 930(m) 880(s) cm^{-1}

NMR (CCl_4) 60 MHz

δ	multiplicity	groups	integrals
1.6 o	Singlet	Two Methyl	6 protons
2.1o	Singlet	Thiol	1 proton
7.1o	Multiplet	Phenyl	5 protons

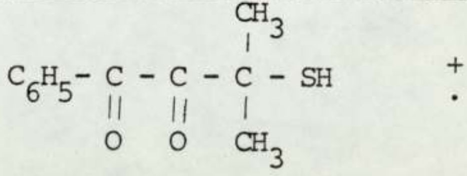
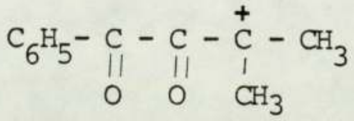
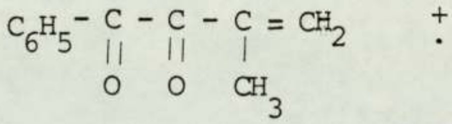
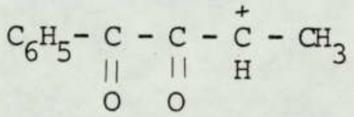
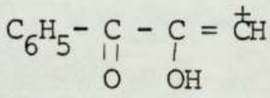
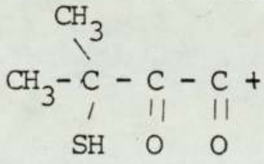
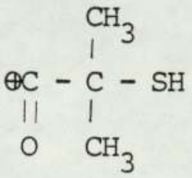
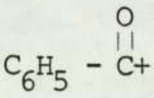
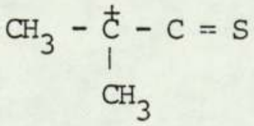
4 - a -11- water in the presence of hydrochloric acid .

Hydrochloric acid (25 ml) IN was added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one. The reaction mixture was stirred at 50° for four days and the product was then extracted several times with ether. The ethereal solution was washed with water, collected and dried over anhydrous sodium sulfate . The ether was removed using a rotary evaporator. The resulting yellow liquid was distilled to give 3-mercapto-3-methyl-1-phenyl-1,2-butanedione. b.p. = 65-67°/0.12mm/Hg Yield 81%.

Spectroscopic data were similar to those of (4-a-10).

Table (18)

Mass spectrum of 3-mercapto-3-methyl-1-phenyl-1,2-butanedione .

m/e	Fragment
208	 $\left[C_6H_5-C(=O)-C(=O)-C(CH_3)_2-SH\right]^{+\cdot}$
175	 $C_6H_5-C(=O)-C(=O)-\overset{+}{C}(CH_3)-CH_3$
174	 $\left[C_6H_5-C(=O)-C(=O)-C(CH_3)=CH_2\right]^{+\cdot}$
161	 $C_6H_5-C(=O)-C(=O)-\overset{+}{C}H-CH_3$
147	 $C_6H_5-C(=O)-C(OH)=\overset{+}{C}H$
131	 $CH_3-C(CH_3)(SH)-C(=O)-C(=O)+$
103	 $\oplus C(=O)-C(CH_3)_2-SH$
105	 $C_6H_5-C(=O)+$
79	 $CH_3-\overset{+}{C}(CH_3)-C=S$
77	$C_6H_5^+$

4 - a-12: Water and Oxygen of air

Oxidation of 3-mercapto-3-methyl-1-phenyl-1,2-butanedione.

3 - Mercapto-3-methyl-1-phenyl-1,2-butanedione in water was heated at 40° for two months. The solid was filtered off and recrystallized from petroleum ether (40 - 60°) to give a yellow solid, bis butanedione disulfide. m.p. = 80° Yield = 98%.

Elemental analysis of $C_{22}H_{22}O_4S_2$

	C	H	S
Calculated	63.82	5.31	15.45 %
Found	63.50	5.40	15.40 %

IR (KBr disc)

3100 (w) 3070 (w) 2985 (vw) 2940 (w) 2860 (m)
1705 (s) C=O) 1675 (s) 1600 (m) 1580 (w)
1470 (w) 1450 (s) 1435 (w) 1390 (m)
1305 (w) 1320 (m) 1305 (w) 1285 (s)
1220 (s) cm^{-1}

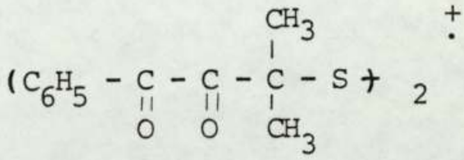
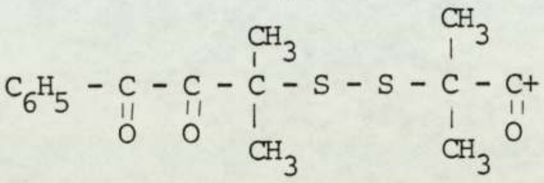
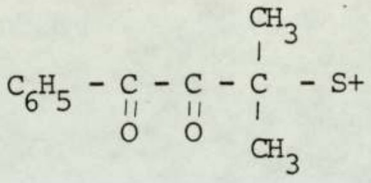
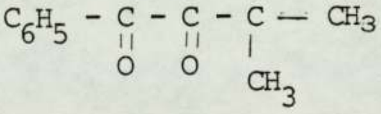
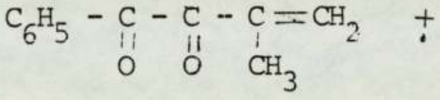
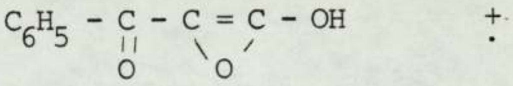
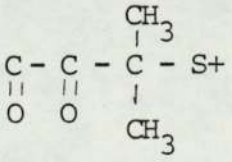
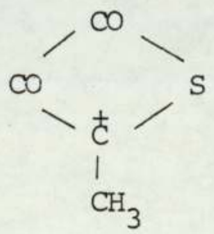
NMR (CCl_4) 60 MHz

δ	multiplicity	groups	integrals
1.6	Singlet	Four Methyl	12 protons
7.4	Multiplet	Two Phenyl	10 protons

The mass spectrum gave a molecular ion at m/e 414 (Table 19).

Table (19)

Mass spectrum of bis-butanedione disulfide

m/e	Fragment
414	 $\left(C_6H_5-\underset{\underset{O}{\Vert}}{C}-\underset{\underset{O}{\Vert}}{C}-\underset{CH_3}{\overset{CH_3}{C}}-S\right)_2^{+\cdot}$
280	 $C_6H_5-\underset{\underset{O}{\Vert}}{C}-\underset{\underset{O}{\Vert}}{C}-\underset{CH_3}{\overset{CH_3}{C}}-S-S-\underset{CH_3}{\overset{CH_3}{C}}-\underset{\underset{O}{\Vert}}{C}{}^+$
207	 $C_6H_5-\underset{\underset{O}{\Vert}}{C}-\underset{\underset{O}{\Vert}}{C}-\underset{CH_3}{\overset{CH_3}{C}}-S^+$
175	 $C_6H_5-\underset{\underset{O}{\Vert}}{C}-\underset{\underset{O}{\Vert}}{C}-\underset{CH_3}{C}-CH_3$
174	 $C_6H_5-\underset{\underset{O}{\Vert}}{C}-\underset{\underset{O}{\Vert}}{C}-\underset{CH_3}{C}=CH_2^{+\cdot}$
146	 $C_6H_5-\underset{\underset{O}{\Vert}}{C}-\underset{\diagdown O \diagup}{C=C}-OH^{+\cdot}$
130	 $\underset{\underset{O}{\Vert}}{C}-\underset{\underset{O}{\Vert}}{C}-\underset{CH_3}{\overset{CH_3}{C}}-S^+$
115	
105	$C_6H_5CO^+$

4 - a - 13 Magnesium

2-Chloro-4,4-dimethyl-2-phenylthietan-3-one (2.26g, 0.01 mole) in dry diethyl ether (15 ml) was added to magnesium (0.37g, 0.012 mole) in dry diethyl ether (15 ml). The temperature was controlled between 27 - 30°. Dry methanol (16 ml) was added to the reaction mixture after thirty minutes. The reaction mixture was stirred overnight at room temperature and the precipitate was filtered off, and the ether was then removed to give a mixture of a solid and a liquid. The solid was filtered off to give fraction 1 and the remaining liquid (Part 2) was found to be benzyl isopropyl ketone.

Part 1

The solid was recrystallized from methanol to give-4,4,4′,4′-tetramethyl-3,3′-dioxo-2,2′-diphenyl-2,2′-bithietanyl.

m.p. = 137 - 139° yield = 55%

IR (KBr disc)

3080(w) 2980(m) 2920(m) 2840(w) 1760(s)(C=O)
1580(w) 1450(s) 1500(s) 1380(m) 1360(m)
1130(s) cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.30	Singlet	Methyl	3 protons
1.55	Singlet	Methyl	3 protons
7.10	Singlet	Phenyl	5 protons

Fraction (2)

IR (thin film)

1710(s)(C=O) cm^{-1}

NMR (CCl_4) 30 MHz

δ	integrals	multiplicity	groups
0.9 - 1.2	6	Doublet	Methyl
1.6 - 3.0	1	Septet	Methine
3.5	2	Singlet	Methylene
7.2	5	Singlet	Phenyl

4 - a - 14: Magnesium in Tetrahydrofuran (THF)

2-Chloro-4,4-dimethyl-2-phenylthietan-3-one (7.75g, 0.034 mole) in THF (30 ml) was slowly added to magnesium (1.4g, 0.058 mole) in THF (30 ml). Methanol (7 ml) was added to the mixture after refluxing for one day. The reaction mixture was allowed to stand at room temperature for two days. Sulfuric acid (1N) was slowly added to the solution at such a rate that the reaction was kept steadily refluxing. The organic compound was extracted using ether and the resulting liquid was distilled after removing the diethyl ether. b.p. = 63°/0.1mm/Hg.

The product was benzyl isopropyl ketone.

IR (thin film)

3075(w) 3040(m) 2980(s) 2940(w) 1710(s) (C=O)

1600(w) 1495(m) 1455(m) 1380(w) 1040(s)

730(s) 690(s) cm^{-1}

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.o	Doublet	Methyl	6 protons
1.6 - 3.o	Septet	Methine	1 proton
3.5	Singlet	Methylene	2 protons
7.2	Singlet	Phenyl	5 protons

4 - a - 15: Zinc

2-Chloro-4,4-dimethyl-2-phenylthietan-3-one (2.63g, 0.011 mole) in dry ether was added to zinc (2.71g, •042 mole). The reaction mixture was stirred for fifteen minutes. Methanol (4.5 ml) was then added to the reaction mixture which was then stirred overnight at room temperature. The organic compound was separated using diethyl ether. The spectroscopic data of the resulting compound were similar to those of (4-a-13).

4 - a-16: Sulfuryl chloride.

Sulfuryl chloride (0.28 mole, 30 ml) was added to 2-chloro-4,4-dimethyl-2-phenylthietan-3-one (0.04 mole, 10g) at room temperature.
Pyridine was slowly added to the mixture and the reaction mixture was then heated at 45-50^{o} for one day (24 hrs). The excess of thionyl chloride was removed using a rotary evaporator. Pyridine hydrochloride was filtered off and the resulting thick oil was eluted from a silica gel column using chloroform.

Fraction 1 was a mixture of fraction 2 and some impurity (side reaction) in low yield.

Fraction 2

The chloroform was removed under reduced pressure. The resulting colourless oil was kept at (-20^{o}) overnight. The white solid was filtered off in the cold to give 1,1,3,4-tetrachloro-3-methyl-1-phenylbutan-2-one. m.p = 35^{o} Yield = 55%

IR (CCl_4)

3080(m)	3040(w)	2980(m)	2940(m)	2880(w)
1730(s) (C=O)		1600(w)	1500(m)	1445(s)
1420(m)		1380(s)	1180(m)	1030(s) cm^{-1}

Elemental analysis of $C_{11}H_{10}Cl_4O$

	C	H
Found	44.9	3.5 %
Calculated	44.o	3.3 %

NMR (CCl_4) 30 MHz

δ	multiplicity	groups	integrals
1.9	Singlet	Methyl	3 protons
3.7 - 4.4	Two Doublet	Methylene	2 protons
7.6	Multiplet	Phenyl	5 protons

The mass spectrum of 1,1,3,4-tetrachloro-3-methyl-1-phenylbutan-2-one showed a molecular ion peak at 298 mass units (Table 20).

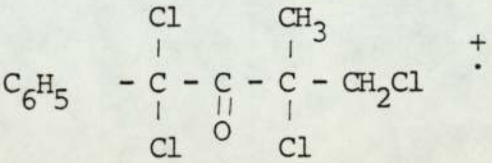
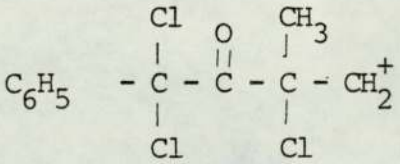
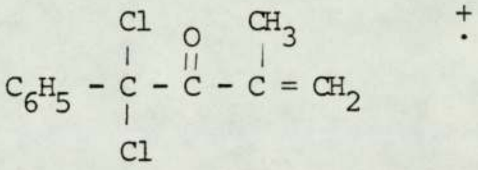
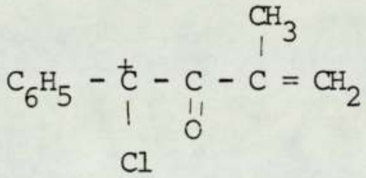
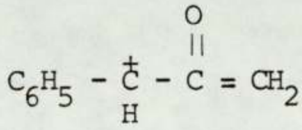
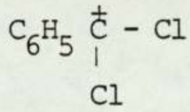
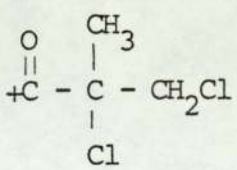
The relative intensity of chlorine isotopes in the molecular ion in the mass spectrum showed the presence of four chlorine atoms in the molecule.

Accurate mass spectrum of1,1,3,4-tetrachloro-3-methyl-1-phenylbutan-2-one of an ion at m/e 298.

m/e	molecular formula	given molecular weight	calculated molecular wt.	error
298	$C_{11}H_{10}Cl_4O$	297.94857	297.94879	0.7ppm

Table (20)

Mass spectrum of 1,1,3,4-tetrachloro-3-methyl-1-phenylbutan-2-one

m/e	Fragments
298, 300, 302, 304, 306	 $[C_6H_5-CCl_2-C(=O)-C(Cl)(CH_3)-CH_2Cl]^{+\cdot}$
263, 265, 267, 269	 $C_6H_5-CCl_2-C(=O)-C(Cl)(CH_3)-CH_2^{+}$
228, 230, 232	 $[C_6H_5-CCl_2-C(=O)-C(CH_3)=CH_2]^{+\cdot}$
193, 195	 $C_6H_5-\overset{+}{C}(Cl)-C(=O)-C(CH_3)=CH_2$
161	 $C_6H_5-\overset{+}{C}H-C(=O)=CH_2$
159, 161, 163	 $C_6H_5\overset{+}{C}(Cl)-Cl$
139, 141, 143	 $^{+}C(=O)-C(CH_3)(Cl)-CH_2Cl$

4 - b : The irradiation of 2,4-dichloro-2,4-dimethylthietan-3-one.

For this experiment a daylight cabinet fitted with a U.V. fluorescent lamp was used. The maximum energy given to the sample is over the range 360 - 380 nm and corresponds to $\sim$700 mw/m^2/nm of mean radiant flux. The sample was dissolved in cyclohexane and placed in a quartz tube and periodically analyzed by infrared spectroscopy.

4 - c: The reaction of 2-chloro-4-ethyl-4-methyl-2-phenylthietan-3-one with Morpholine

Morpholine (1.76g, 0.02 mole) in diethyl ether (20 ml) was added to 2-chloro-4-ethyl-4-methyl-2-phenylthietan-3-one (2.4g, 0.01 mole) in diethyl ether (20 ml) at (15 - 20°). The reaction mixture was stirred for three days at room temperature and the morpholine hydrochloride was filtered off. The ether was evaporated off using a rotary evaporator. The following spectroscopic data were taken before distillation.
The product was 2-ethyl-2-methyl-4-morpholino-4-phenylthietan-3-one.

IR (thin film)

3060(m) 2980(s) 2860(s) 1760(s) $C=O$
1670(w) 1630(w) 1600(w) 1490(m)
1440(s) 1370(m) 1270(s) 1110(s)
800(s) cm^{-1}

NMR (CCl_4) 60 MHZ

δ	multiplicity	groups
0.8 - 1.1	Multiplet	Ethyl
1.45	Singlet	Methyl (1)
1.7	Singlet	Methyl (2)
2.5	Triplet (d)	Methylene-$CH_2{-}N{-}CH_2{-}$
2.95	Singlet (b)	Methylene-CH_2CH_3
3.65	Triplet (d)	Methylene-$CH_2{-}O{-}CH_2{-}$
7.75	Multiplet	Phenyl

The ratio of protons of Methyl (1) to Methyl (2) is 0.73. The resulting yellow oil was eluted from an alumina (Al_2O_3) column using carbon tetrachloride.

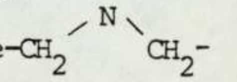
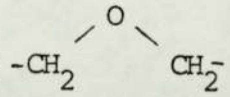
<u>Fraction 1</u> IR and NMR spectra were similar to the above.

<u>Fraction 2</u>

IR (thin film)

1760(s)(CO) 1670(w) 1600(w) 1440(s) cm^{-1}

NMR (CCl_4) 60 MHz

δ	multiplicity	groups
0.8-1.2 o	Multiplet	Ethyl
1.5 o	Singlet	Methyl (1)
2.5 o	Singlet (b)	Methylene- $CH_2\diagup^{N}\diagdown CH_2-$
2.95	Singlet (b)	Methylene-CH_2-CH_3
3.65	Triplet (d)	Methylene  $-CH_2\diagup^{O}\diagdown CH_2-$
7.75	Multiplet	Phenyl

Comparing the NMR spectra before chromatography with fraction 2, showed the disappearance of some of the peaks at 0.8 - 1.1 ppm and a peak at 1.7 ppm (Methyl 2). Figure 10 shows the ^{13}C nuclear magnetic resonance spectrum of 2-ethyl-2-methyl-4-morpholino-4-phenylthietan-3-one and morpholine.

```
           30
       2.4412
       0.0005
  2487.7929
           18

FREQ(HZ)    PPM     INT
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 2922.36  129.789  1426
 [illegible] 129.162  3833
 [illegible] 128.317  4987
 [illegible] 128.308  5165
 2861.32  127.088   594
 2834.47  125.088   397
 1770.01   78.562   296
 1738.28   77.154   338
 1706.54   75.745   326
 1621.09   71.952   223
 1503.98   66.758  1732
 1494.16   66.317  5886
 1450.15   64.367  1786
 1105.95   49.083   452
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  969.23   43.019  [illegible]
  852.05   37.818   247
  749.51   33.267  1854
  712.89   31.641   857
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    0.00    0.000   612
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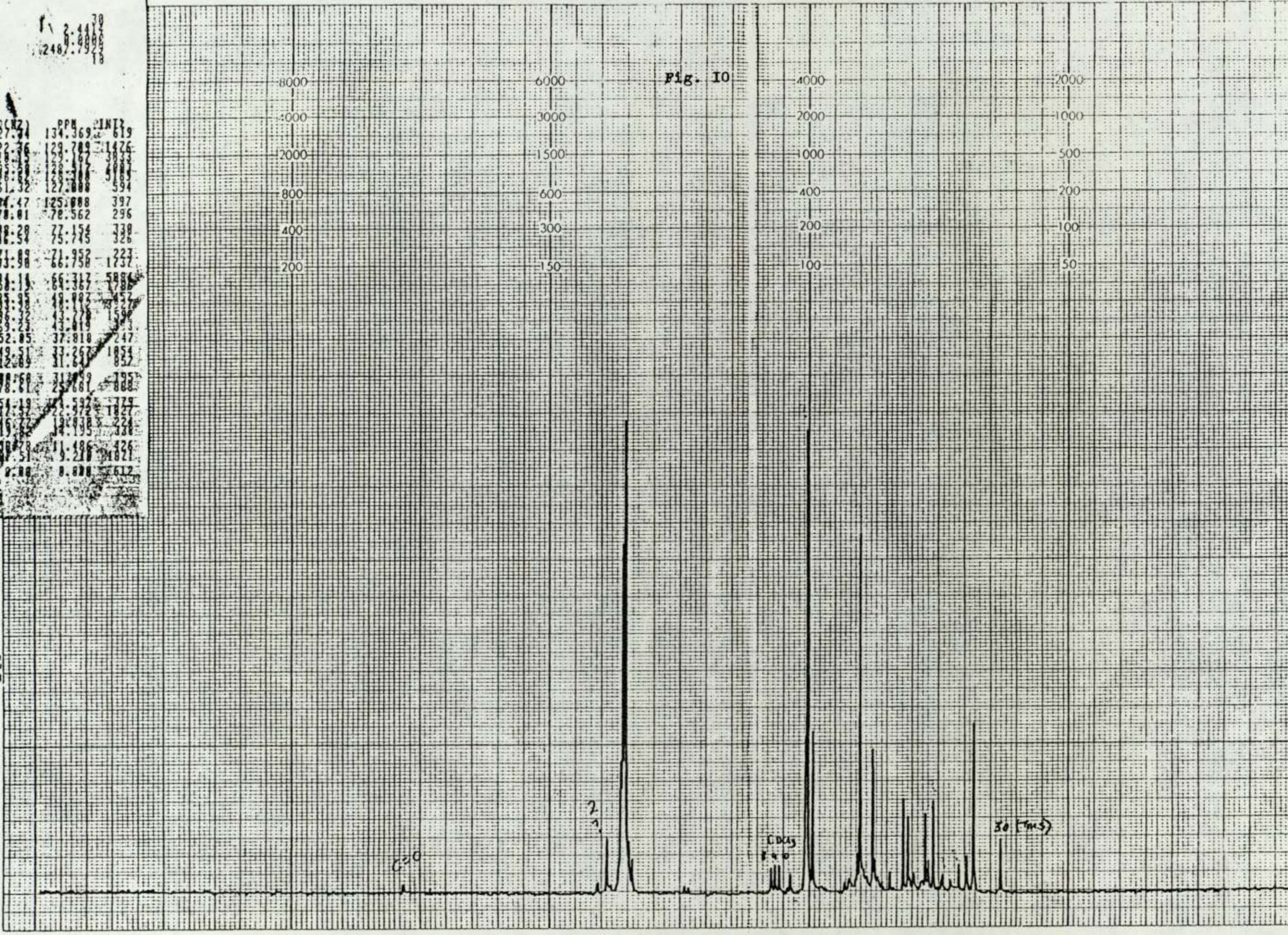
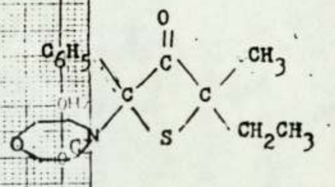


FX 90Q

CHART NO.
SAMPLE



SOLVENT CDCl₃ TUBE mm
CONCENTRATION
REFERENCE TMS
TEMPERATURE

NUCLEUS ¹³C
OBS 22.5 MHz
LOCK ☑ D ☐ F ☐ H
IRR
OFFSET
OBS
IRR
PULSE ☑ SINGLE ☐ MULTI
WIDTH μSEC
INTERVAL 1 SEC
REPETITION 1 SEC

DATA POINTS 8000
WINDOW
NO. OF PULSES 2500

SPECTRAL WIDTH 10,000
RF GAIN
AMPLITUDE

DECOUPLING
☐ CW ☑ NOISE ☐ PARTIAL
☐ HOMO ☐ HETERO
POWER
LOCK
RF LEVEL
RF GAIN
AMPLITUDE

DATE 21/5/81
OPERATOR
REMARKS

JEOL

Supplied by Nuclear Magnetic Resonance Ltd., Magnetic House, Scrubbs Lane, Bledlow Ridge, High Wycombe, Bucks.

2

4 - d: The reaction of 4-benzylidene-2,2-dimethylthietan-3-one with thionyl chloride in the presence of pyridine

4-Benzylidene-2,2-dimethylthietan-3-one (2g, 0.01 mole) was refluxed for eight days with a large excess of thionyl chloride (10 ml) and a small amount of pyridine (0.1 ml). The excess of thionyl chloride was evaporated off. A thick oil was eluted from a silica gel column using petroleum ether (40 - 60°) and diethyl ether in a 10:1 ratio. The resulting fraction 1 was kept at -20° overnight and at room temperature for two days. The yellow solid was washed with a small amount of cold petroleum-ether (40 - 60°) to give 2-chloro-2-(α-chloro-α-chlorosulfenylbenzyl)-4,4-dimethylthietan-3-one. m.p. = 65 - 67°. Yield = 50%

IR (KBr disc)

3075 (vw) 2985 (w) 2940 (w) 2860 (vw) 1780 (s) (C=O)
1450 (s) 1370 (w) 1190 (m) 1130 (s) 950 (m)
770 (s) 730 (s) 700 (s) 650 (m) cm^{-1}

NMR (CCl_4) 60 MHz

δ	multiplicity	groups	integrals
1.35	Singlet	Methyl	3 protons
1.85	Singlet	Methyl	3 protons
7.65	Singlet	Phenyl	5 protons

The mass spectrum of 2-chloro-2-(α-chloro-α-chlorosulfenylbenzyl)-4,4-dimethylthietan-3-one showed a molecular ion peak at 340 mass units (Table 21).

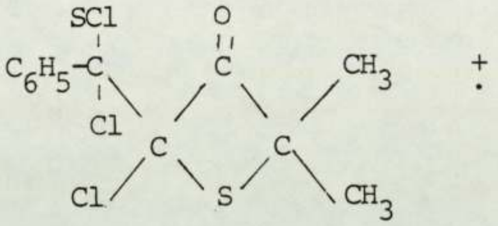
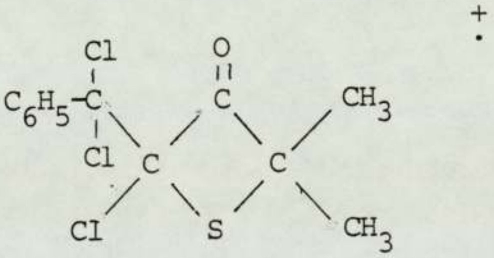
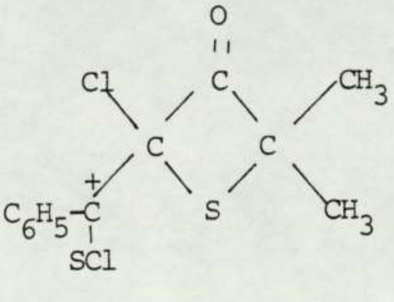
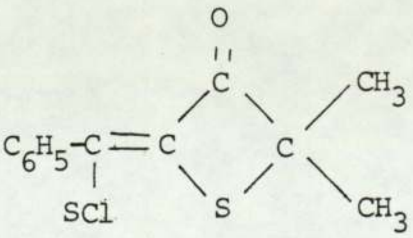
Accurate mass spectrum of ions at m/e340 and 308

m/e	molecular formula	calculated molecular weight	given molecular wt.	error
308	$C_{12}H_{11}Cl_3OS$	307.96082	307.95961	3.9ppm
340	$C_{12}H_{11}Cl_3OS_2$	339.93305	339.93168	4.0ppm

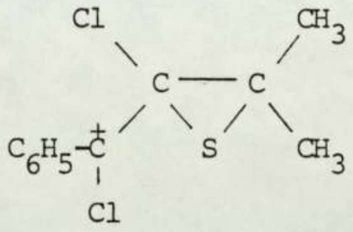
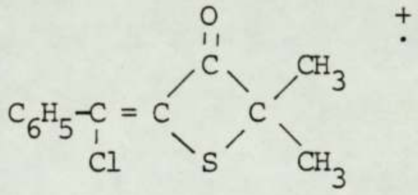
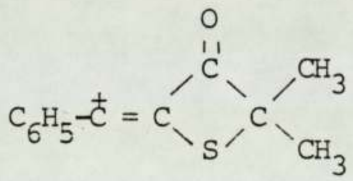
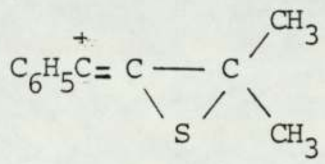
The existence of three chlorine atoms in the molecule was confirmed by measuring the relative intensity of peaks at M, M+2, M+4 and M+6.

Table (21)

Mass spectrum of 2-chloro-2-(α-chloro-α-chlorosulfenylbenzyl)-4,4-dimethylthietan-3-one.

m/e	Fragments
340,342,344, 346	
308, 310, 312, 314	
305, 307, 309	
270, 272	

(Table 21) continued

m/e	Fragments
245, 247, 249	
238, 240	
203	
175	

CHAPTER 5

PREPARATION OF SULFINYL CHLORIDES AND THIETANONES AND THE REACTIONS OF KETONES AND SULFINYL CHLORIDES

Page

CHAPTER 5

DISCUSSION

CHAPTER FIVE

Introduction .

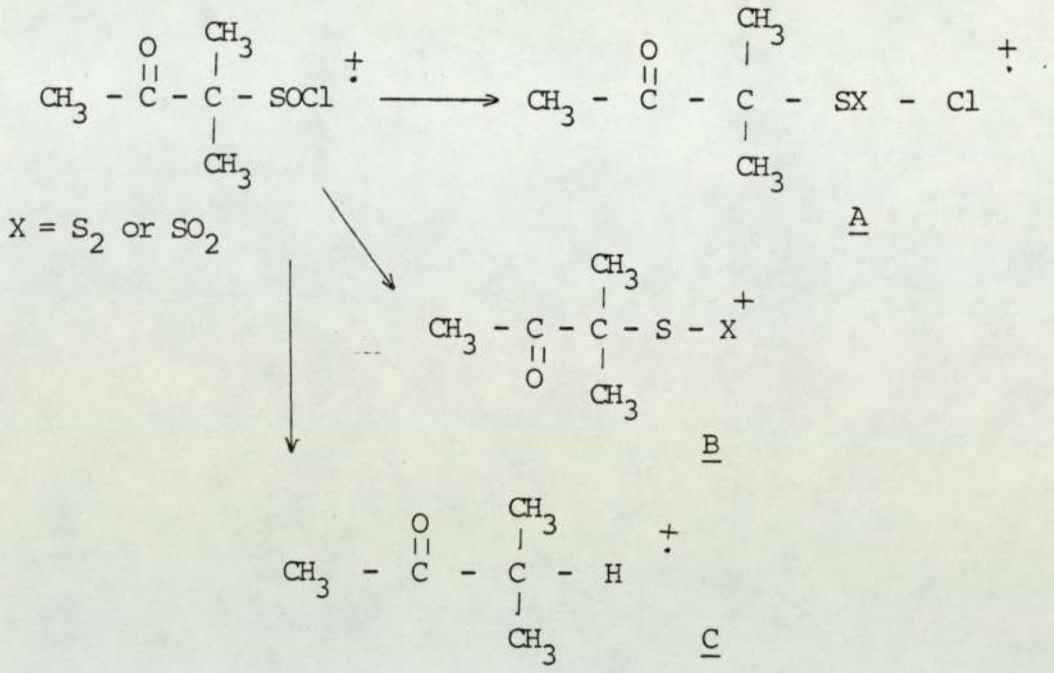
In this part the structures, stereochemistry of the products and the possible mechanism of the reactions will be discussed.

5 - Preparation of sulfinyl chlorides and thietanones and the reactions of ketones and sulfinyl chlorides.

5 - a : The sulfinyl chlorides .

Ketones on treatment with thionyl chloride give a variety of products depending upon the number of α, $\acute{\alpha}$-protons present. Ketones containing one alpha proton afforded β-ketosulfinyl chlorides. β-Ketosulfinyl chlorides are intermediates in the reaction between certain ketones and thionyl chloride. Ketones with three protons, two in the α-position and one in the $\acute{\alpha}$-position, e.g. ethyl isopropyl and benzyl isopropyl ketone when treated with thionyl chloride give the chlorothietan-3-ones as a final product and β-ketosulfinyl chlorides have been proposed(16) as intermediates. Isopropyl methyl ketone with four protons, three in the α-position and one in the $\acute{\alpha}$-position, and di-isopropyl ketone with two protons, one in the α-position and one in the $\acute{\alpha}$-position gave the β-keto sulfinyl chlorides. The β-ketosulfinyl chlorides of these ketones are stable enough for isolation before further reaction with thionyl chloride. In all the sulfinyl chlorides studied the sulfoxide absorption in the infrared gave a strong band at 1150 $\pm$ 5 cm^{-1}. The proton magnetic resonance spectra of sulfinyl chlorides provided much information for the assignment of the structure. In most of the sulfinyl chlorides the gem-dimethyl group absorbed as two singlets instead of one, this doubling is due to a diastereotopic effect. The pattern of the spectrum changes with changes in the polarity of the solvent employed(39). The optical stability of the chlorosulfinyl group has been studied (77,34,35). The tetrahedral sulfur atom of the chlorosulfinyl group S O Cl can induce magnetic nonequivalence of the geminal groups (39). Thus the sulfinyl chloride group acts as an asymmetric group and causes nonequivalence in the molecule. Vandervlies (78) concluded that two structural requirements are necessary for the "doubling effect" to take place in some isopropyl esters. Firstly the molecule should possess an asymmetric centre and secondly it should possess a phenyl ring or alternatively an aromatic solvent such as benzene should be used. Gupta et al. (39). have found that these conditions are unnecessary. Thus in certain cases quite large shifts are found for purely aliphatic sulfinyl chlorides in the absence of any solvent.

The mass spectroscopy of sulfinyl chlorides does not appear to have been reported in the literature. Meyerson et al. (79) and his co-workers suggested that cyclic sulfoxides usually lose sulfur monoxide in the mass spectrum. The mass spectrum of the β-ketosulfinyl chlorides does not generally show a parent ion, e.g. the mass spectrum of 3-chlorosulfinyl-3-methylbutan-3-one does not show a parent ion. The major fragment produced is ketone (C) and peaks at $\frac{m}{e}$ 216,218 and 181 are possible due to A and B respectively, X is S_2 or SO_2. There is no firm evidence to support the existence of SO_2 or S_2.



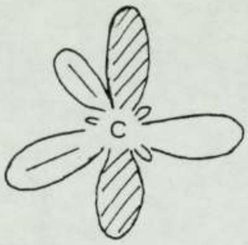
Analysis using gas-liquid chromatography was not successful for the determination of the purity of the β-ketosulfinyl chlorides because of the high reactivity of these compounds. Finally β-ketosulfinyl chlorides decompose very quickly at room temperature in a similar manner to alkanesulfinyl chlorides$^{(80)}$. However, β-ketosulfinyl chlorides can be stored for several months at low temperatures (-20°).

5 - b : Thietanones .

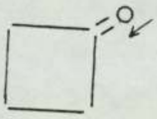
Certain ketones with thionyl chloride give the four-membered ring of the 2-chlorothietan-3-ones. The carbonyl absorption of these compounds has a band at 1780 cm^{-1} in the infrared spectrum. The increase in frequency occurs because the carbonyl vibration in the 2-chlorothietanone is strongly coupled to the C-C single bond vibrations. A carbon-carbon bond adjacent to a carbonyl group has almost sp^2 character. According to Baeyer when closed chains or rings were formed, the valence bonds of carbon atoms become diverted from their normal tetrahedral direction and therefore possess angle strain.

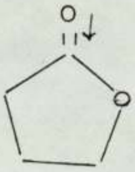
The ring strain shifts the absorption value to a higher wave number. Smaller rings require the use of more p-character in making the C-C bonds meet the requisite small angles (recall the trend $sp = 180^\circ$, $sp^2 = 120^\circ$ $sp^3 = 109^\circ$, $sp^{>3} = < 109^\circ$). This removes p-character from the sigma bond of the double bond, but gives it more s-character, thus strengthening and stiffening the double bond. The force constant k is then increased and the absorption frequency increases.

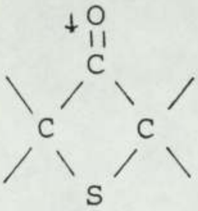
increased p character
due to angle requirements

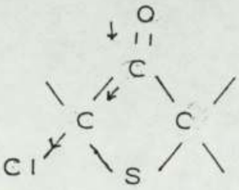


increases s character
strengthens s bond of
m system.









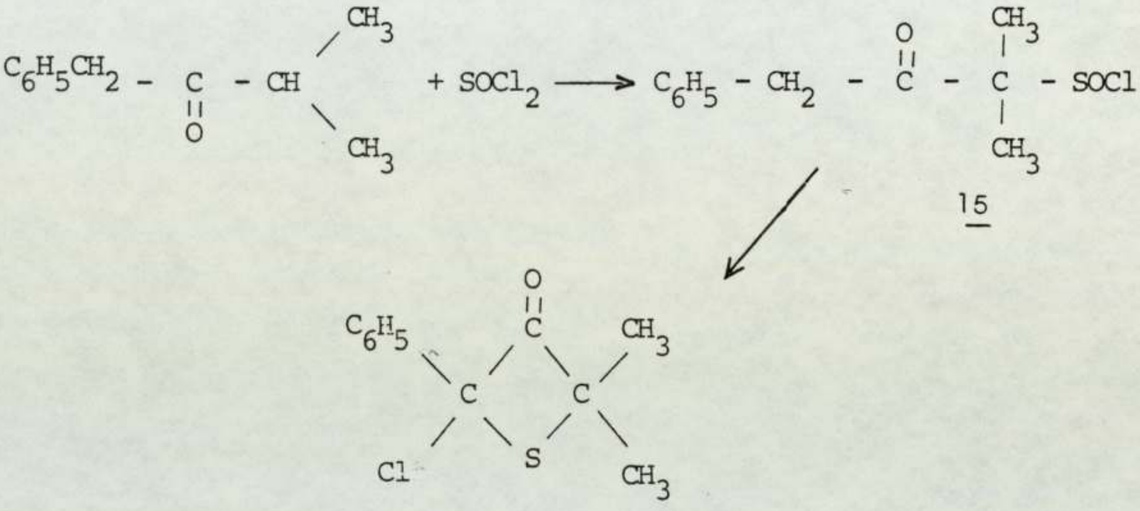
strain and electron
withdrawing effect raises
C = o frequency.

1715 ⟶ 1760

strain raises C = O frequency

5 - b - 1 : 2-Chloro-4,4-dimethyl-2-phenylthietan-3-one .

The treatment of benzyl isopropyl ketone with thionyl chloride gave the 2-chlorothietan-3-one 16.



15

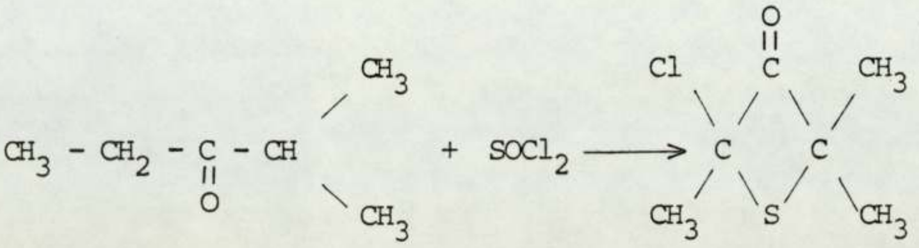
16

Spectroscopic data confirmed structure 16. Infrared spectra showed a peak at 1780cm^{-1} due to the carbonyl group. Protons of the two methyl and phenyl groups absorbed at δ = 1.4, 1.75 and 7.35ppm respectively in the nuclear magnetic resonance spectrum. The mass spectrum of the 2-chlorothietan-3-one 16 gave molecular ion peaks at 226 and 228 mass units confirming the formation of the 2-chlorothietanone 16. The relative intensity of peaks 226 and 228 was 1:3 which showed the existence of one chlorine atom in the molecule.

The intensity ratio of molecular ion clusters due to halogen isotopes may be calculated by the expansion $(a + b)^n$. (a is the abundance of the lighter isotope, b is the abundance of the heavier isotope and n is the number of the halogen atoms)

5 - b - 2 : 2-Chloro-2,4,4-trimethylthietan-3-one .

The treatment of ethyl isopropyl ketone with thionyl chloride gave <u>55</u>.



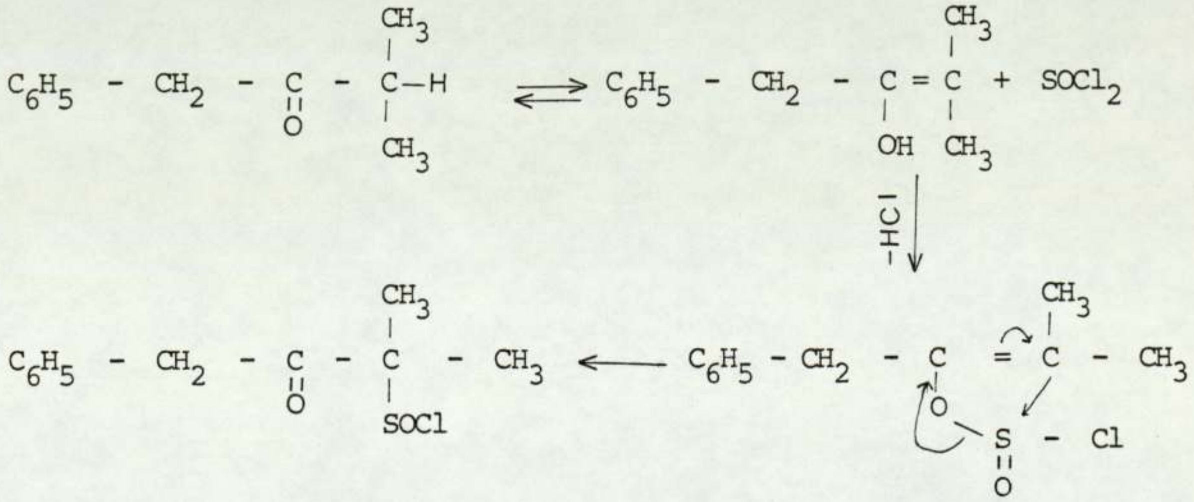
<u>55</u>

The position of the carbonyl group of the chlorothietanone <u>55</u> is at 1780cm^{-1} in the infrared spectrum and the chemical shifts of the protons of the three methyl groups are at δ = 2, 1.85 and 1.58 ppm in the nuclear magnetic spectrum.

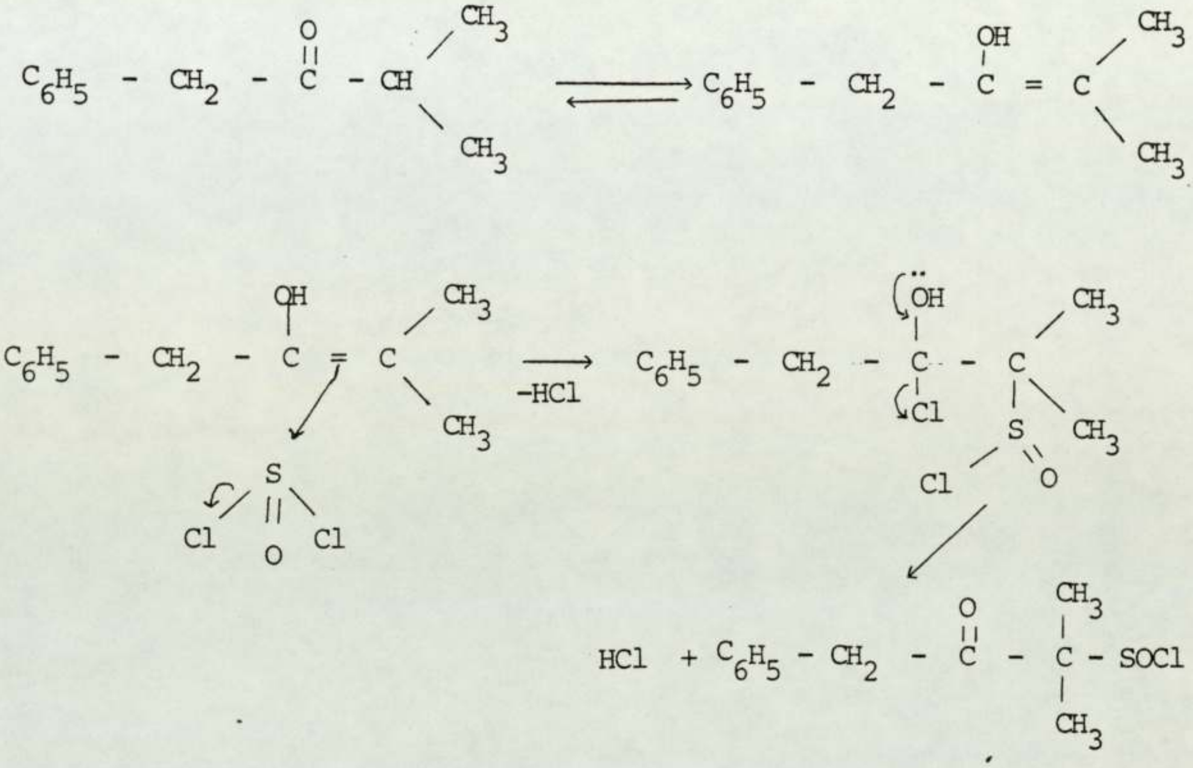
The structure of the unsaturated compound formed from the reaction of ethyl isopropyl ketone with thionyl chloride in the presence of pyridine at 0° (see Page 40) is thought to be 2,2-dimethyl-4-methylenethietan-3-one. However, the anomalous NMR spectra (Page 40) showing two peaks for the two methyl groups must cast some doubt on this.

Ethyl and benzyl isopropyl ketones with thionyl chloride give the β-ketosulfinyl chlorides in the first stage. The reaction might go by scheme a or b.

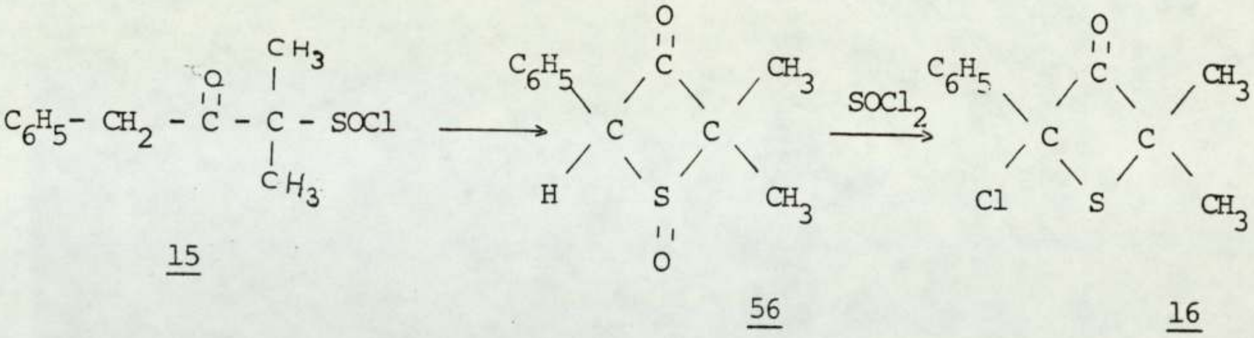
Scheme a : Electrophilic attack at the hydroxyl group of the enol.



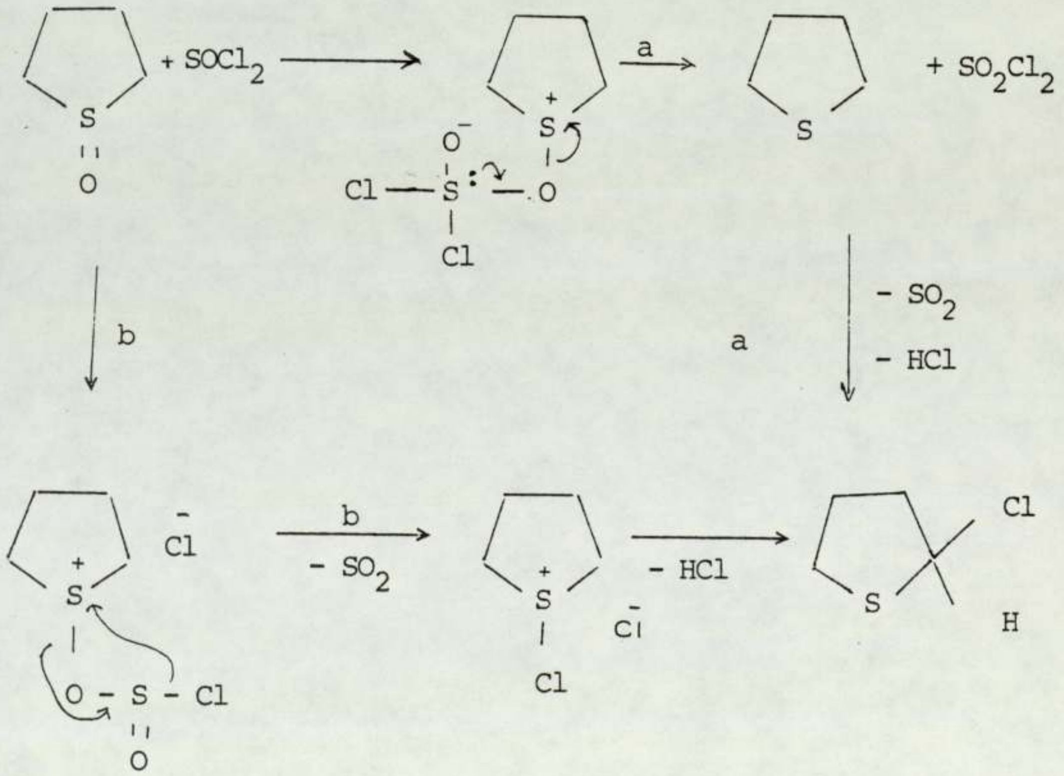
Scheme b : Nucleophilic attack of the carbon-carbon double bond.



Gupta(21) suggested the formation of the β-ketosulfinyl chlorides occurs via the enolic form. Evidence which supported the theory that attack occurred at the enol form came from the treatment of isobutyronitrile and isopropyl acetate with thionyl chloride(21). However, in both scheme a and b the enolic form has an important role and the existence of a carbonyl group attached to the isopropyl group is essential for the formation of the sulfinyl chlorides, but there is no firm evidence to support scheme a or scheme b. The β-ketosufinyl chloride <u>15</u> cyclizes to the chlorothietan-3-one <u>16</u>. Cyclization probably proceeds via the cyclic sulfoxide which is thus converted to the chlorothietan-3-one by an Hell-Volhard-Zelinsky process(81, 82).

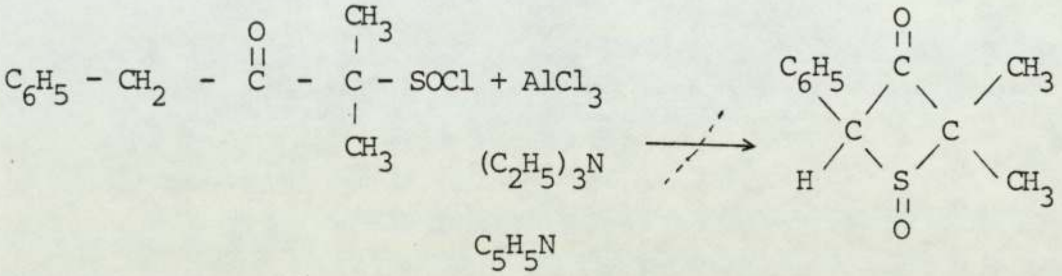


Bordwell and Pitt$^{(81)}$ examined the reaction of sulfoxides with thionyl chloride. Thiacyclopentane 1-oxide with thionyl chloride gave 2-chlorothiacyclopentane. They suggested the reaction goes via mechanism a or b.



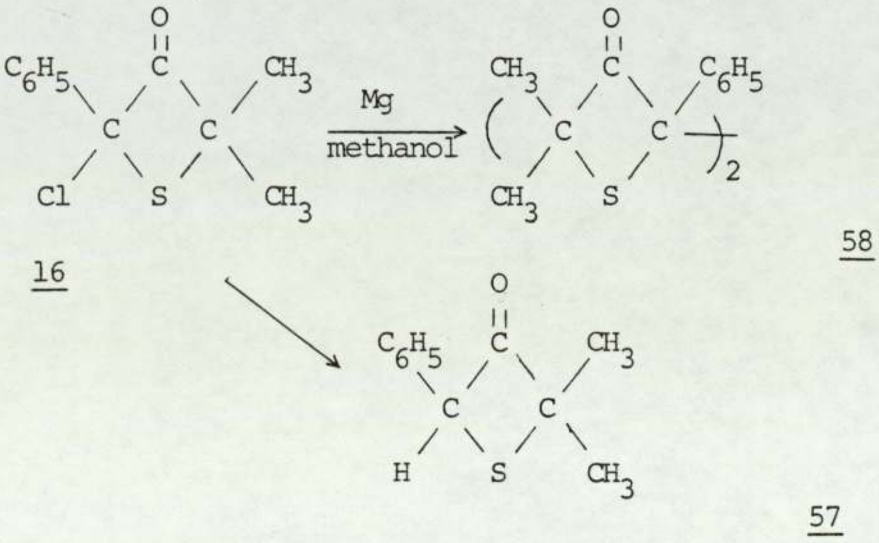
We tried to prepare the cyclic sulfoxide 56 by methods I and II so that the mechanism could be further studied.

I. An attempt was made to prepare 56 by treating the sulfinyl chloride 15 with aluminium chloride, triethylamine or pyridine.

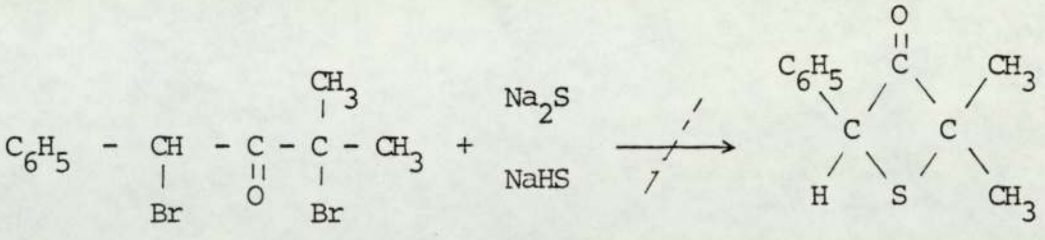


II. It was also envisaged that the cyclic sulfoxide 56 could be formed by oxidation of 2, 2-dimethyl-4-phenylthietan-3-one 57. Several methods were used for the preparation of the thietanone 57 and they are discussed below.

1 - The reaction of 2-chloro-4, 4-dimethyl-2-phenylthietan-3-one with magnesium followed by adding methanol to the mixture, the product was the dithietanone 58 instead of thietanone 57. (The structure of the thietanone 58 is discussed in p.198).



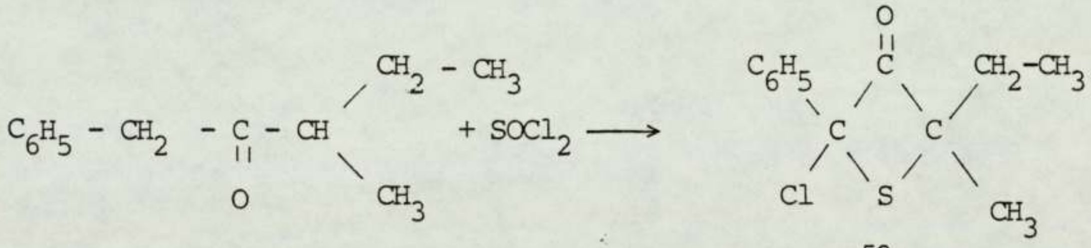
The treatment of the dibromoketones with sodium sulfide or sodium hydrosulfide did not give thietanone 57 (see page 148)



57

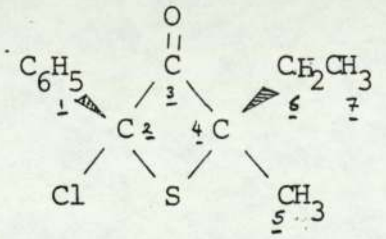
5 - b - 3 : 2-Chloro-4-ethyl-4-methyl-2-phenylthietan-3-one.

3-Methyl-1-phenylpentan-2-one was treated with thionyl chloride. The resulting compound could be the 2-chlorothietan-3-one 59.

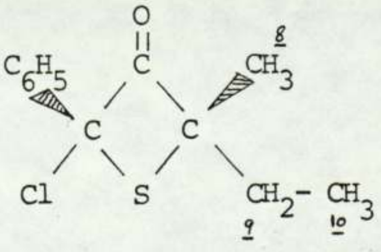


59

The infrared spectrum of the resulting compound showed a band at 1790 cm^{-1} due to a carbonyl group. The position of the carbonyl group in the infrared spectrum confirmed the formation of a four-membered ring. The carbonyl absorption of 2-chlorothietanone 59 is shifted about 70cm^{-1} to a higher wave number when compared with the absorption of the carbonyl group of benzyl ispropyl ketone (starting material) because of the effect of strain in small rings (Baeyer theory) and a halogen atom on carbon-2. The product 59 was expected to have two isomers 59a and 59b.

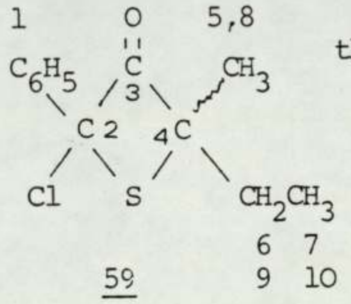


59a



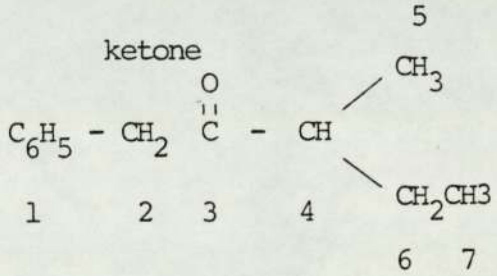
59b

The stereoisomer assignments can be made from nuclear magnetic resonance spectra. The nuclear magnetic resonance of the product showed a multiplet at $\delta = 0.75 - 1.35$ppm due to the ethyl group, two singlets at $\delta = 1.5$ and 1.9 ppm due to methyl protons (C-5 and C - 8) and a peak at $\delta = 7.3$ ppm due to the phenyl group. The chemical shift of methylene protons (C-6) seems to be the same as that of the methyl at (C-7) and the chemical shift of the protons of the methyl (C-5) was down field compared to that of the methylene (C-6). These resulting shifts were unexpected. The relative ratio of peaks at 1.9 and 1.5 is almost 1:1. This evidence shows that an equal percentage of both isomers is present. However, proton nuclear magnetic resonance spectra of the product did not distinguish sufficiently between the ethyl chemical shift for 59a and 59b (carbons 6, 7, 9 and 10). This information, however can easily be obtained from ^{13}C nuclear magnetic resonance spectroscopy and hence the presence of the isomers can be verified. The ^{13}C chemical shift (in parts per million) of carbons in structure 59 are in page 133 . There are different chemical shifts for carbons 5, 6, 7, 8, 9 and 10 respectively which is evidence for the presence of two isomers.



59

thietanone



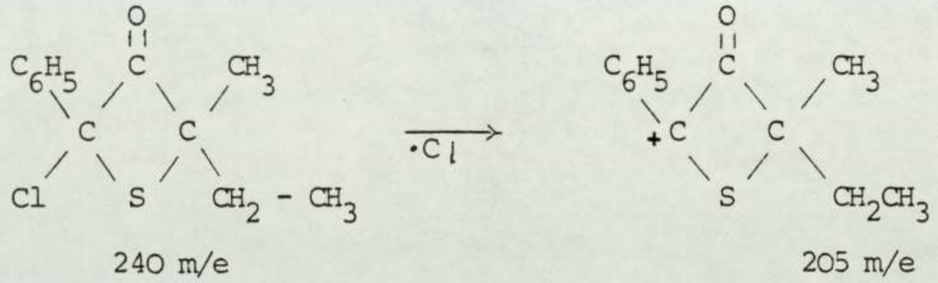
The chemical shift of the carbons in the ketone and thietanone (ppm)

^{13}C	Ketone	Thietanone
1	129.49	129.93
2	47.03	33.05
3	211.74	190.17
4	48.54	31.97
(5	(16.03	(18.96
(8	(-	(18.64
(6	(25.9	(25.79
(9	(-	(24.49
(7	(11.59	(9.75
(10	(-	(9.53

It was not possible to separate the two isomers from the mixture by distillation because of their instability to heat or by column choromatography because of their instability to air.

The alkyl substituted aliphatic ketones whether acyclic or cyclic have carbonyl chemical shifts in the range 200-220 ppm(83-85). α-Substitution by a halogen atom results in a marked shielding of carbonyl resonances(86,87). Placement of an sp^2 centre α to a carbonyl function causes a shielding of as much as 10ppm(85-88). The chemical shift of carbonyl carbon in 3-methyl-1-phenylpentan-2-one is 211.74ppm and the chemical shift of carbonyl carbon in 2-chloro-4-ethyl-4-methyl-2-phenylthietan-3-one is 190ppm.

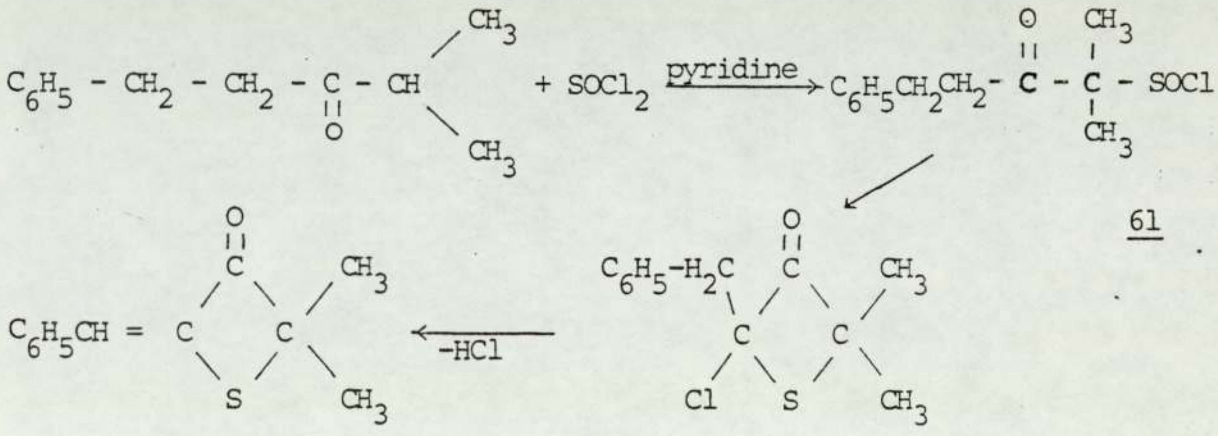
α, $\acute{\alpha}$-Substitution by halogen and sulfur causes a shielding of 20ppm as expected. The mass spectra of chlorohydrocarbons has been studied by a number of workers[(89)]. It has been found that tertiary alkyl chlorides can lose the chlorine atom very easily and the relative abundances of the mass ion of M-Cl is 100%. Identification of the parent ions in alkyl chlorides is not usually possible. The mass spectrum of 2-chloro-4-ethyl-4-methyl-2-phenylthietan-3-one did not show a parent ion at 240 mass units but gave a peak at 205 mass units due to structure 60 formed by the loss of a chlorine atom.



60

5 - b - 4 : 4-Benzylidene-2, 2-dimethylthietan-3-one

Treatment of 2-methyl-5-phenylpentan-3-one with thionyl chloride in the presence of pyridine gave 4-benzylidene-2, 2-dimethylthietan-3-one 17.



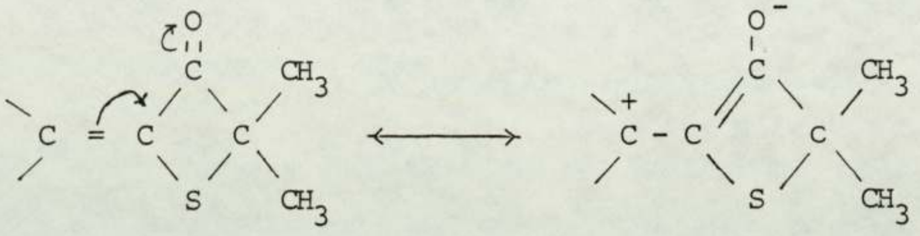
61

17

62

The first stage gave the sulfinyl chloride 61 which was then converted by further thionyl chloride to the chlorothietanone 62 and then dehydrohalogenation could ensue to give the unsaturated compound 17. The thietanone 62 has not been isolated but is presumed to be an intermediate in the formation of thietanone 17. Bands found at

1610 and 1755cm^{-1} are due to a carbon-carbon double bond (C=C) and a carbonyl group respectively. The conjugation effect in the benzylidenethietanone 17 lowers the carbonyl wave number. The C = C bond adjacent to a carbonyl group results in delocalization of the electrons in the carbonyl and double bonds. This conjugation increases the single bond character of the C = O bond and, hence, lowers its force constant, resulting in a lowering of the frequency of carbonyl absorption.

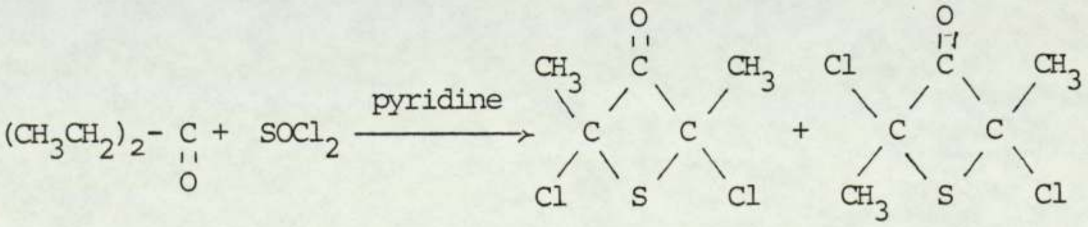


17

A nuclear magnetic resonance spectrum showed singlets at δ = 1.75 and 7.45ppm. The relative ratio of the two peaks was 1:1. The peak at δ = 1.75ppm was due to the two methyl groups and the peak at δ = 7.45ppm was due to the protons of the benzylidene group. The accurate mass spectrum of the product confirmed the formation of the thietanone 17.

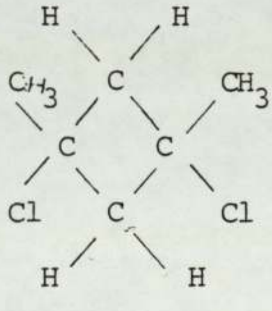
5 - b - 5 : 2,4-Dichloro-2,4-dimethylthietan-3-one.

Diethyl ketone in the presence of pyridine gave 2,4-dichloro-2, 4-dimethylthietan-3-one 21.



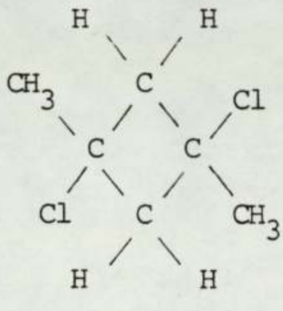
21A 21B

The infrared spectrum showed a peak at 1795cm^{-1} due to the carbonyl group of a four-membered ring. The mass spectrum of the product showed molecular ion peaks at 184, 186 and 188 mass units. An accurate mass spectrum gave a molecular formula of $C_5H_6Cl_2OS$ which is in agreement with the proposed structure. Two singlet peaks at $\delta = 2.2$ and $\delta = 2.35$ ppm in the nuclear magnetic resonance spectrum were due to the methyl groups in the isomers A and B. Two singlet peaks in the nuclear magnetic resonance spectrum confirmed the formation of the cis - and trans-isomers. The mixture of cis- and trans-isomers could not be separated by distillation or chromatography. The question is which of the two peaks at $\delta = 2.2$ and 2.35 ppm belongs to which isomer. Stereochemical studies of many cyclic (four, five membered rings) and olefinic (disubstituted ethylenes) compounds can be found in the literature(89 - 100). From these studies it has been concluded that the protons of trans-isomers are generally downfield compared to the protons of the cis-isomer e.g. the chemical shift of the methyl protons of cis- and trans-1, 3-dichloro-1, 3-dimethylcyclobutane are at $\delta = 1.69$ and 1·86 ppm respectively(101).



$\delta = 1.69$ppm

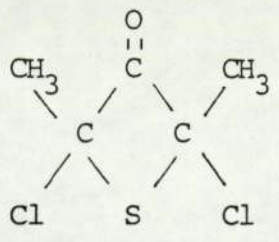
cis



$\delta = 1.86$ ppm

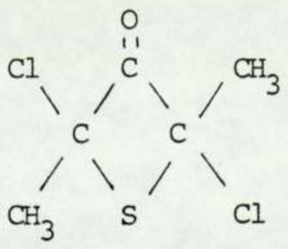
trans

Thus the chemical shift of the cis- and trans-methyl protons of 2, 4-dichloro -2,4-dimethylthietan-3-one are probably at $\delta = 2.2$ and 2.35 ppm respectively.



$\delta = 2.2$ppm

cis



$\delta = 2.35$ppm

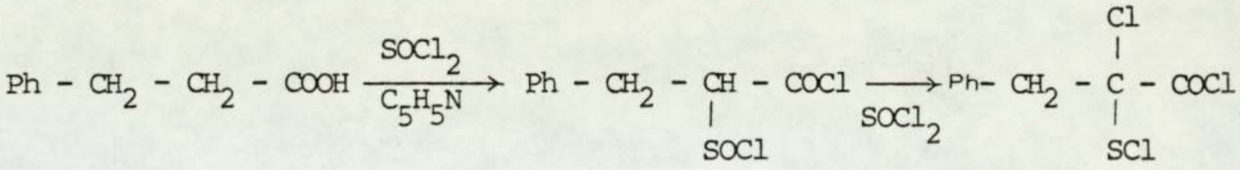
trans

The percentage of each isomer was determined by the relative intensity of the two peaks. The relative ratio of the peaks at $\delta = 2.35$ and $\delta = 2.2$ppm could be changed by using different conditions for their preparation (experimental 2-d-4). In the first condition (at room temperature) the relative ratio of peaks at $\delta = 2.35$ to $\delta = 2.2$ ppm was 3:2 and the melting point was 40 - 42^{O}. In the second condition (using heat) the relative ratio of peaks at $\delta = 2.35$ to $\delta = 2.2$ppm was 7:3, melting point was 47-50^{O}. In general the melting and boiling points of trans-compounds are usually higher than cis-compounds (102-103). The higher melting point (using the second condition) suggested a larger percentage of the trans-isomer and the nuclear magnetic resonance spectrum of the product in these conditions showed an increase in the intensity of the peak at $\delta = 2.35$ppm which suggest the peak at $\delta = 2.35$ppm was due to the trans-isomer. However, cis- and trans-2, 3-dichloro-2, 3-dimethylbutene-2 have been separated but there is no difference between the chemical shifts of the trans- and cis- methyl protons (103).

$\delta_{cis} = 2.2$ppm $\delta_{trans} = 2.2$ppm.

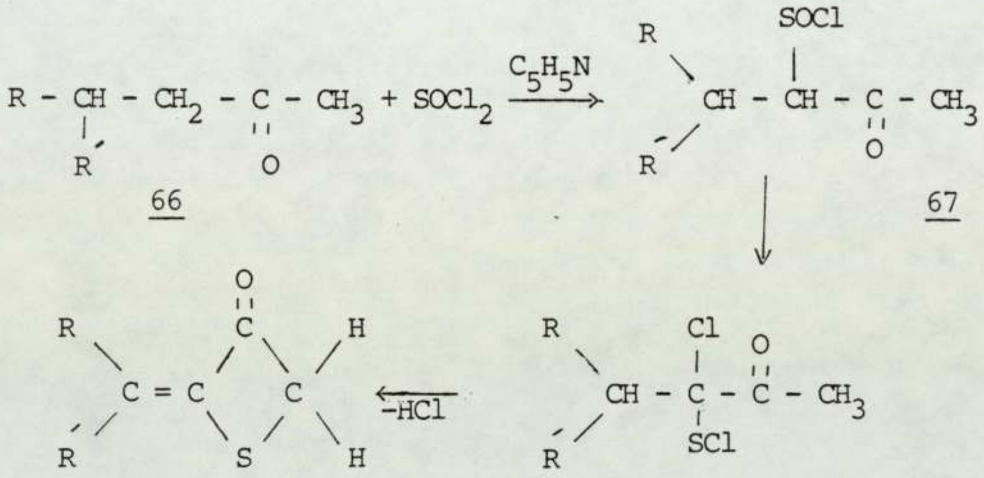
When the mixture of the cis- and trans- isomers was photo-irradiated, cis and trans isomerisation did not take place and the light catalyzed the decomposition of the thietanone.

Ketones containing two protons in the α-position on treatment with thionyl chloride gave the α-chloro-α-sulfenyl chloride derivatives. Higa et al. (104-106) studied the reaction of certain ketones and carboxylic acids with thionyl chloride. The carboxylic acid 63 and the Ketone 66 with thionyl chloride gave the α-chloro-α-sulfenyl chlorides 65 and 68 respectively.



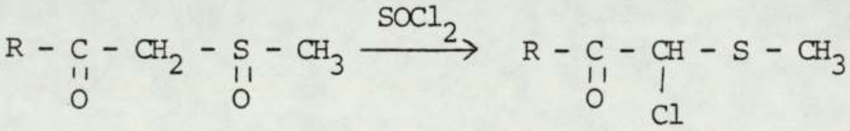
$$\mathrm{Ph-CH_2-CH_2-COOH \xrightarrow[C_5H_5N]{SOCl_2} Ph-CH_2-\underset{\displaystyle SOCl}{\underset{|}{CH}}-COCl \xrightarrow[SOCl_2]{} Ph-CH_2-\overset{\displaystyle Cl}{\overset{|}{\underset{\displaystyle SCl}{\underset{|}{C}}}}-COCl}$$

63 64 65



66 67 68

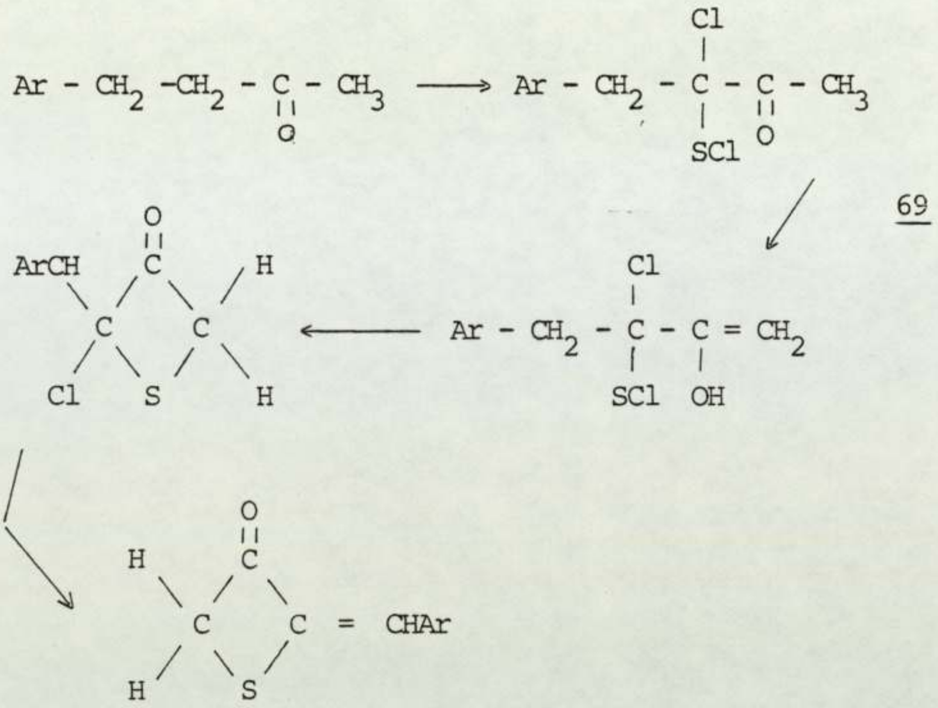
The sulfinyl chlorides 64 and 67 have been proposed$^{(104-106)}$ as intermediates in the formation of the sulfenyl chlorides 65 and 68. A lot of work has been done which confirms the reduction of sulfoxide by thionyl chloride$^{(107,\ 81)}$, e.g. the β-ketosulfoxide$^{(107)}$ below.



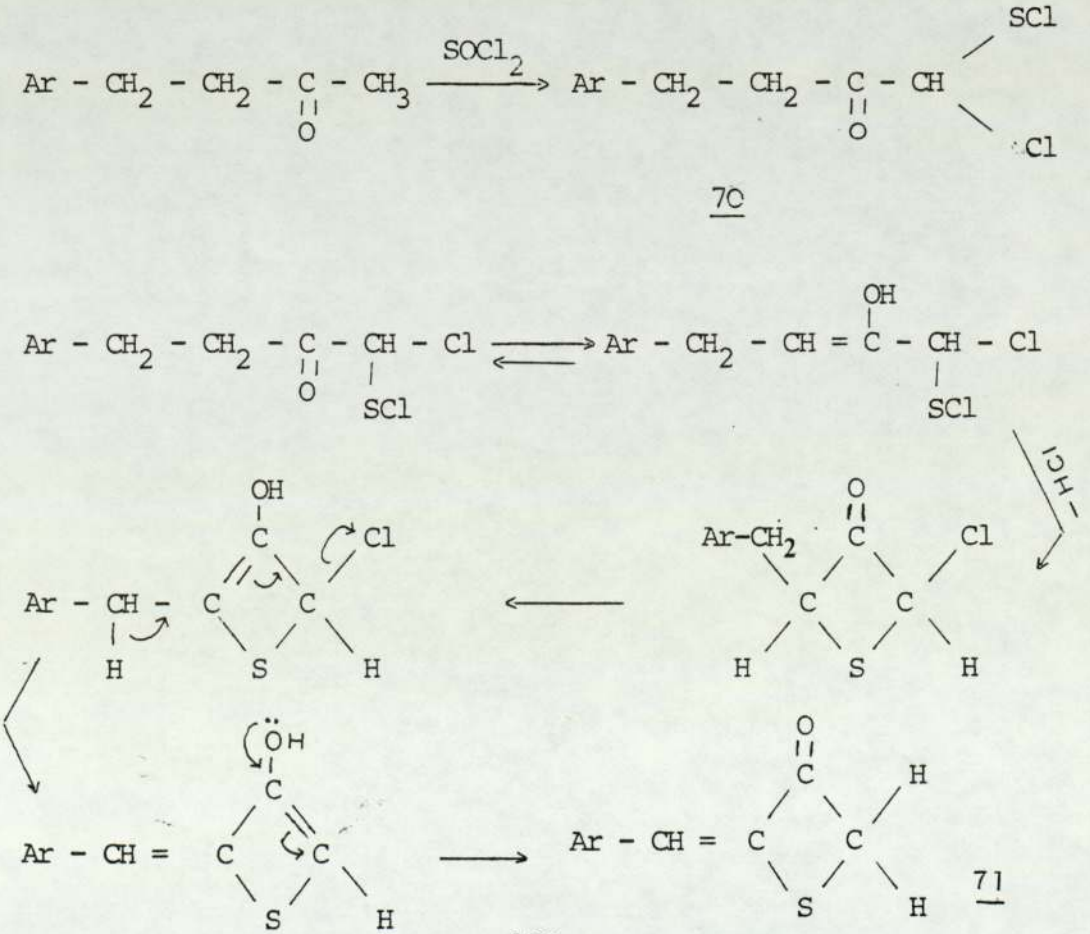
$$\mathrm{R-\underset{\displaystyle O}{\underset{\|}{C}}-CH_2-\underset{\displaystyle O}{\underset{\|}{S}}-CH_3 \xrightarrow{SOCl_2} R-\underset{\displaystyle O}{\underset{\|}{C}}-\underset{\displaystyle Cl}{\underset{|}{CH}}-S-CH_3}$$

Krubsack et al.$^{(23)}$ have investigated the mechanism of the formation of the thietan-3-one. There are three possible routes for the formation of the thietanone$^{(23)}$.

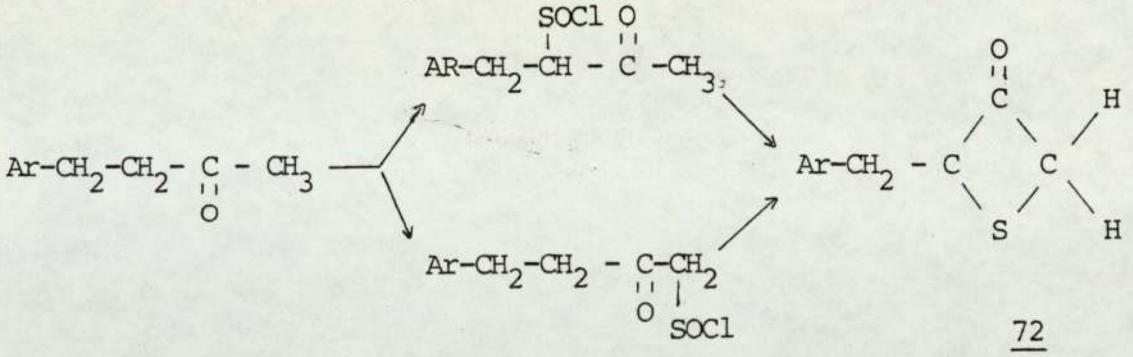
A :



B : If for some reason electrophilic addition occurred at the methyl carbon rather than at the methylene carbon then the following route would be possible.



C : The third possibility is.

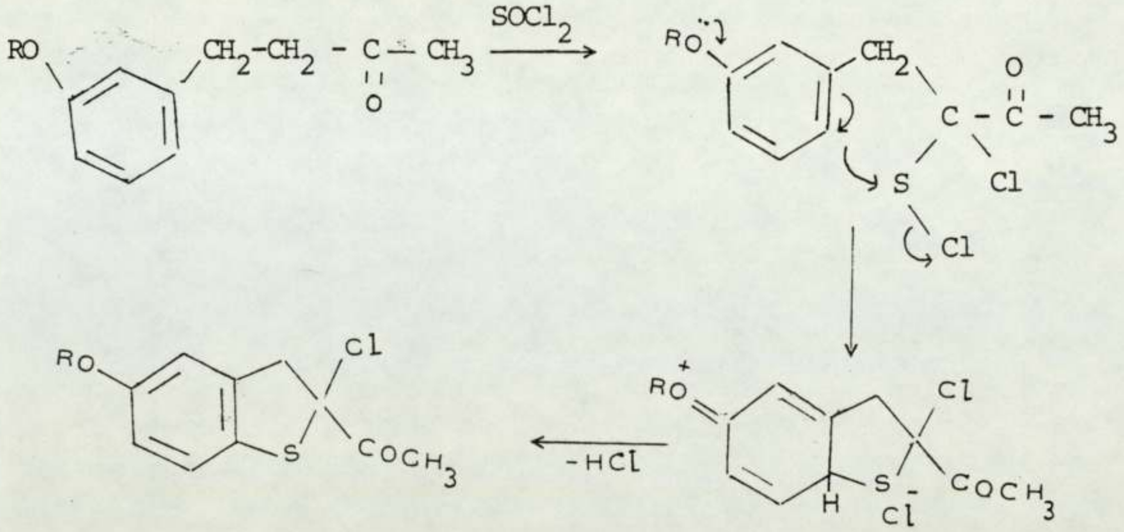


72

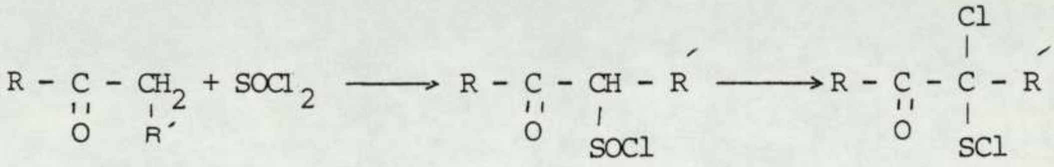
$\underline{72} \longrightarrow \underline{71}$

Route A has been found to be correct. The mechanism of the reaction was detected by chemical reactivity. The reaction of certain ketones with thionyl chloride gave benzothiophene. If the chlorosulfenyl chloride 70 was the intermediate, it was not obvious how a benzothiophene could be formed. However, if the chlorosulfenyl chloride 69 was the intermediate then it should be possible to explain the formation of the thiophene.

Krubsack et al.(23) found that benzothiophenes form readily in a thionyl chloride reaction when (a) there is an electron - withdrawing substituent at the benzylic carbon atom (β to the carbonyl group) or (b) there is a strongly electron-donating ring substituent that can interact through resonance with sulfur atom of the sulfenyl chloride group in a nucleophilic displacement reaction.



Finally the absence of thietanone formation in the case of the 3-hydroxyl-derivative suggests the exclusive operation of the first (a) rather than the second (b) mechanism. Pizey and Symeonides$^{(18)}$ have studied the reaction of certain ketones containing two protons in the α-position. Treatment of the propiophenones 73 with thionyl chloride rapidly gave the sulfinyl chlorides 74 which were slowly converted to the α-chloro-α-sulfenyl chlorides 75. The preparation of the α-chloro-α-sulfenyl chloride confirmed the views of Krubsack et al.$^{(23)}$.



$$R-\underset{\underset{O}{\|}}{C}-\underset{\underset{R'}{|}}{CH_2}+SOCl_2 \longrightarrow R-\underset{\underset{O}{\|}}{C}-\underset{\underset{SOCl}{|}}{CH}-R' \longrightarrow R-\underset{\underset{O}{\|}}{C}-\overset{\overset{Cl}{|}}{\underset{\underset{SCl}{|}}{C}}-R'$$

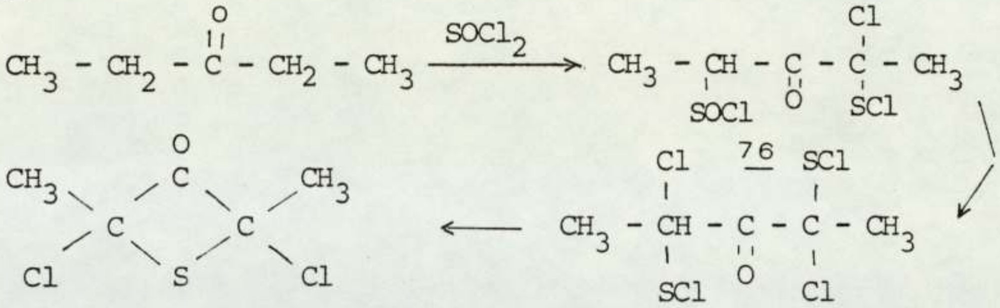
73 74 75

R = C_6H_5 R' = Me

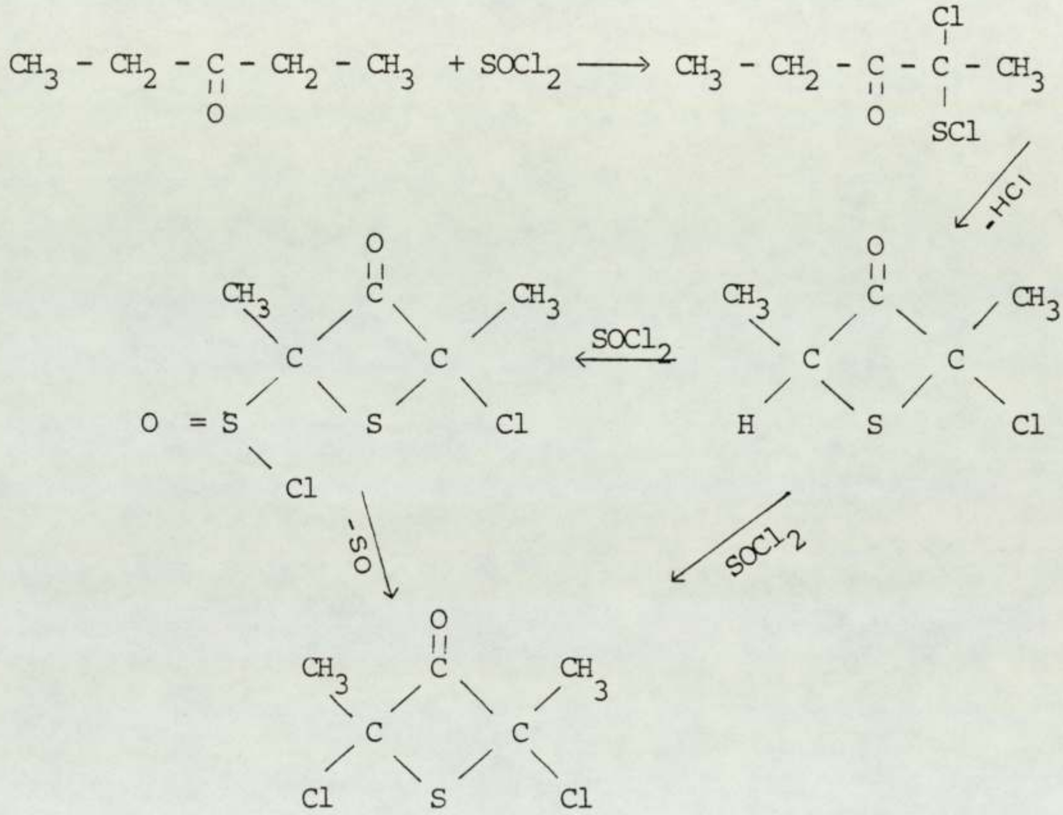
R = $m\text{-}O_2NC_6H_4$ R' = Me

On these grounds, we were able to suggest a mechanism for the reaction of the diethyl ketone with thionyl chloride. This reaction gave the α-chloro-α-sulfenyl chloride in the first stage which then underwent conversion to-2, 4-dichloro-2, 4-dimethylthietan-3-one. The mechanism of the reaction might be by route A or B.

A:



B :



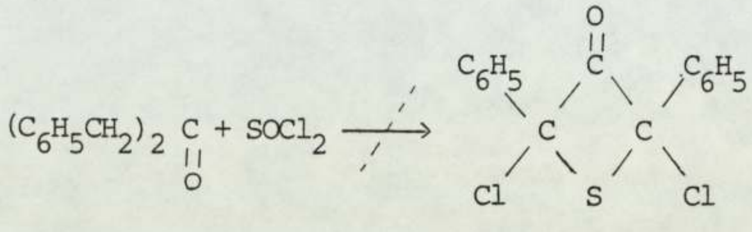
The evidence below supports the theory that the reaction goes by route B.

I: It is found that thionyl chloride is able to chlorinate methyl, methylene or methine protons attached to sulfur atom (see p.161).

II: 2-Chlorosulfinyl-2, 4-dimethyl pentan-3-one with thionyl chloride in the presence of pyridine did not give-2, 4-dichlorosulfinyl-2, 4-dimethylpentan-3-one hence, it is less likely to form the intermediate of -2-chloro-2-chlorosulfenyl-4-chlorosulfinylpentan-3-one 76 .

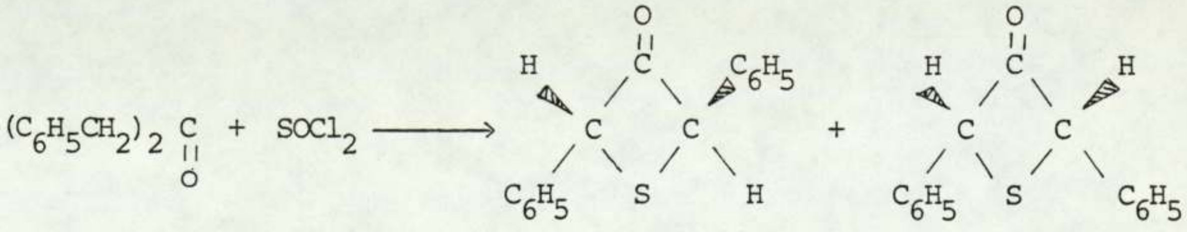
5 - b - 6 : 2, 4-Diphenylthietan-3-one

Dibenzyl ketone was treated with thionyl chloride in the presence of pyridine. The product was expected to be the dichlorothietanone 77, since the treatment of diethyl ketone with thionyl chloride gave 2, 4-dichloro-2, 4-dimethylthietan-3-one 21 (see section (5-b-5) .



77

A peak at 1790cm^{-1} in the infrared spectrum supported the idea of the formation of a four-membered ring. However the nuclear magnetic resonance spectrum did not agree with the structure of the dichlorothietanone 77. According to structure 77 phenyl protons should appear at δ = 7.3 ppm and there should be no other protons in the system. However, in the spectrum recorded, there were two methine protons at δ = 4.1 ppm, in addition to the ten phenyl protons at δ = 7.65 ppm (The chemical shift of methine protons attached to three different electron-withdrawing group, carbonyl, sulfur and phenyl group is at δ = 4-4.5ppm, e.g. the methine proton of thietan-3-one-1-dioxide$^{(108)}$. Therefore the product obtained from this reaction could be either of the structures 78a or 78b. The mass spectrum of the product did not give a parent ion at 240 mass units as expected, this fact was rationalized in terms of the instability of the product.

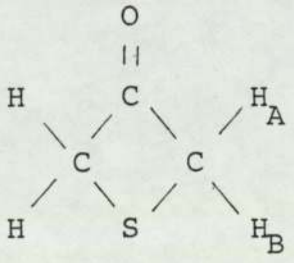


78a 78b

The product is unstable, and the colourless liquid changed to a white solid in a short period of time. The melting point of the white solid is 70° and the infrared spectrum of the solid compound showed a peak at $1700cm^{-1}$. The appearance of a peak at $1700cm^{-1}$ and disappearance of a peak at $1790cm^{-1}$ showed the decomposition of the four membered ring. The mass spectrum of the product (colourless liquid) gave mass ions similar to these of the solid compound (decomposition). Steric hindrance prevented the chlorination and formation of a α-chloro-α-chlorosulfenyl compound as an intermediate.

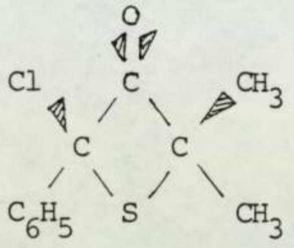
5 - b - 7 : Investigation of the planarity of thietanone and thietanone derivatives.

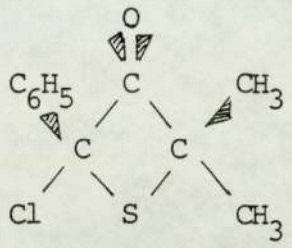
Thietan-3-one was prepared by Mayer and Funk(109) and the planarity of this compound was studied using the far infrared and microwave region(63). Investigation of the nuclear magnetic resonance spectrum of thietan-3-one confirmed the planarity of the thietanone. The nuclear magnetic resonance spectrum of thietan-3-one gave a singlet at α = 4.2ppm(110). If the ring was not planar, there would be a chemical shift difference between the two gem protons A and B of the thietanone.



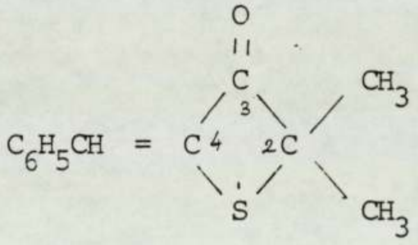
If the ring was planar the chemical shift of the protons A and B would be equivalent.

The nuclear magnetic resonance spectrum of 2-chloro-4, 4-dimethyl 2-phenylthietan-3-one showed two singlet peaks for the methyl protons which is agreement with ring planarity. If the ring was not planar protons of the thietanone 16 in the nuclear magnetic resonance spectrum should show four singlet peaks, two singlets for structure 16a and two singlets for structure 16b. (Figures 11 and 12).


16a


16b

For further evidence the thietanone 17 was studied. This has only one group attached to carbon-4.



17

The nuclear magnetic resonance spectrum showed only one singlet corresponding to the six methyl protons thus confirming that this molecule is planar. (Figures 11 and 12).

Fig. 11

Photograph of a model of 2,2,4,4-tetramethylthietan-3-one.

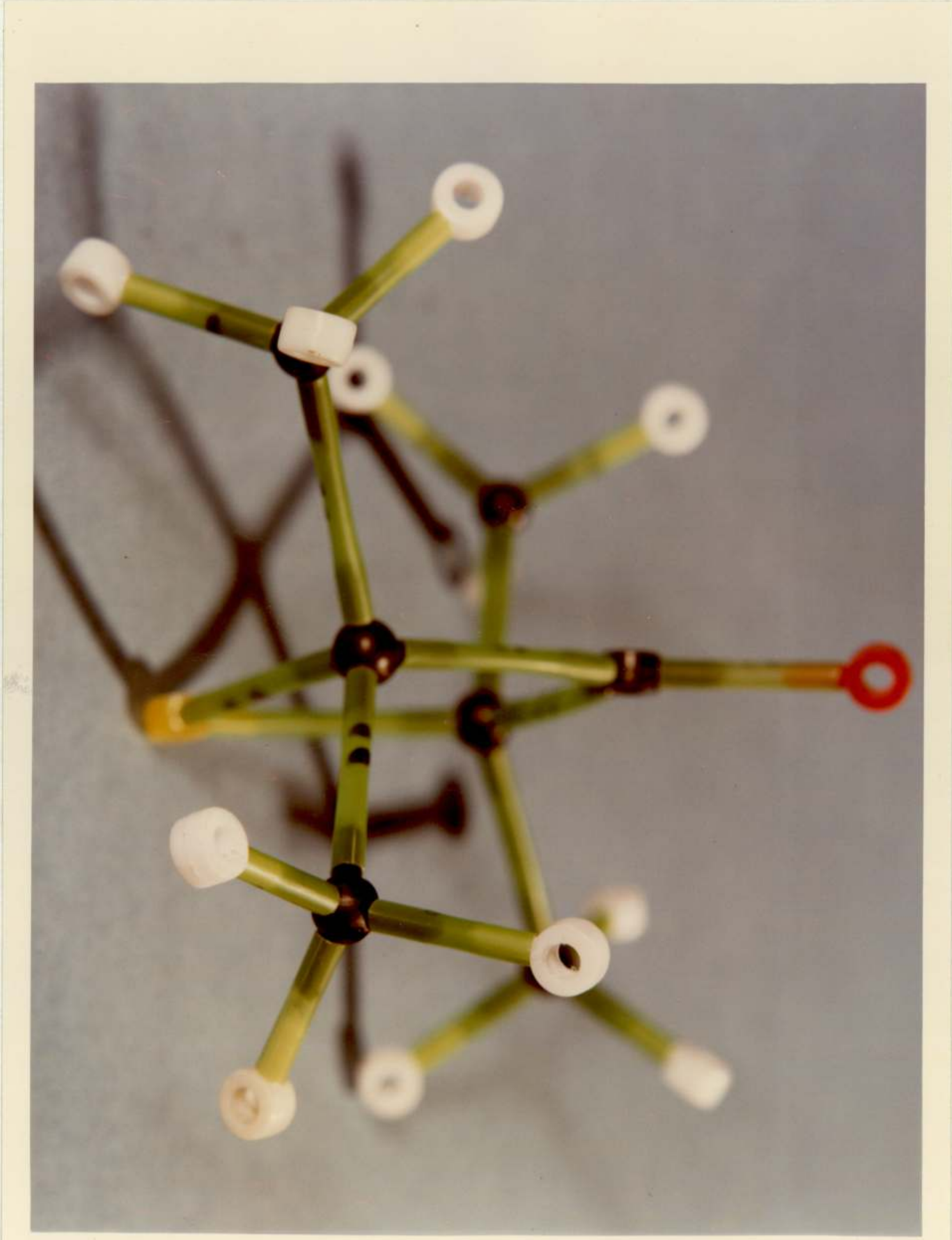
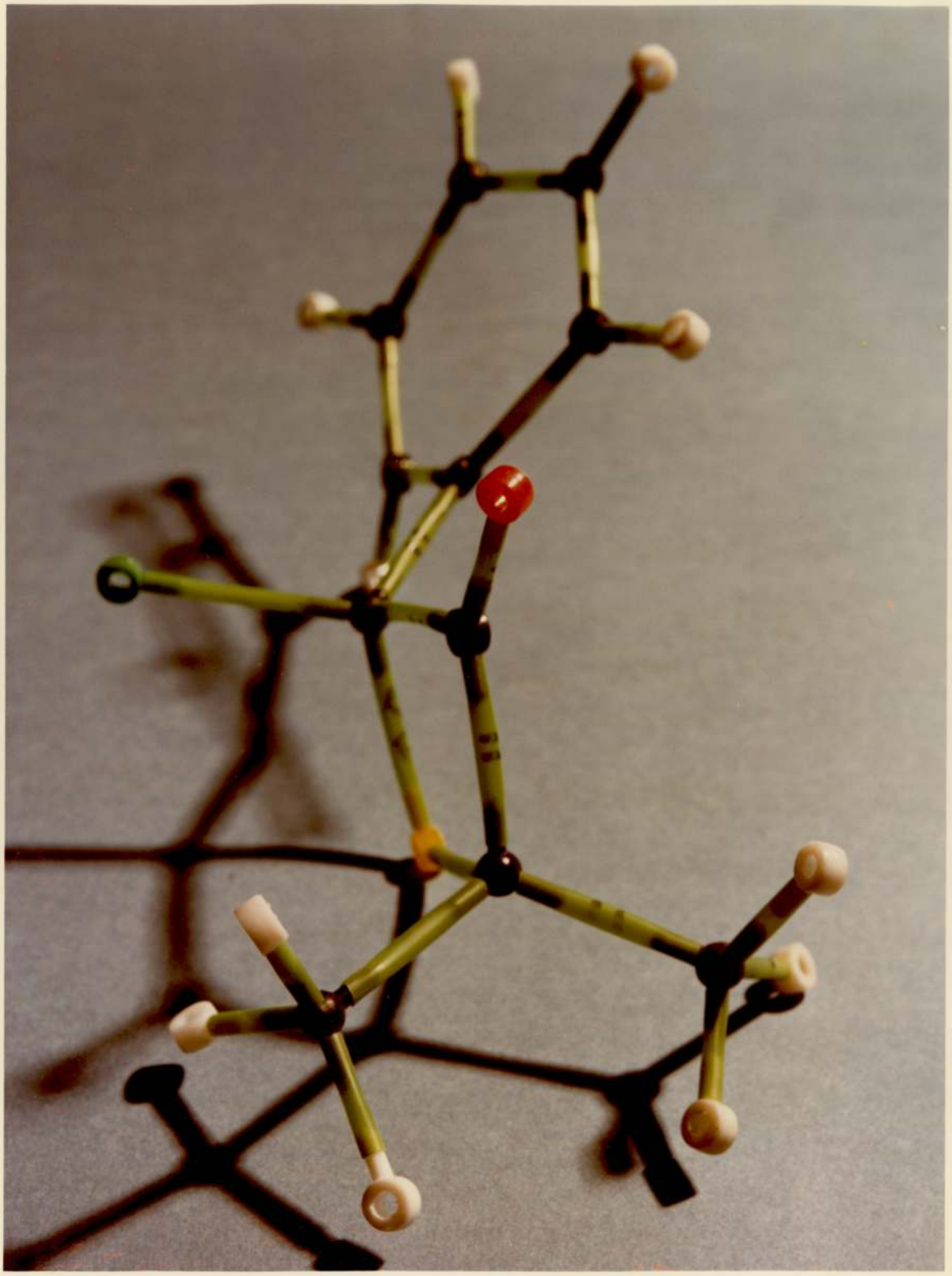


Fig. 12

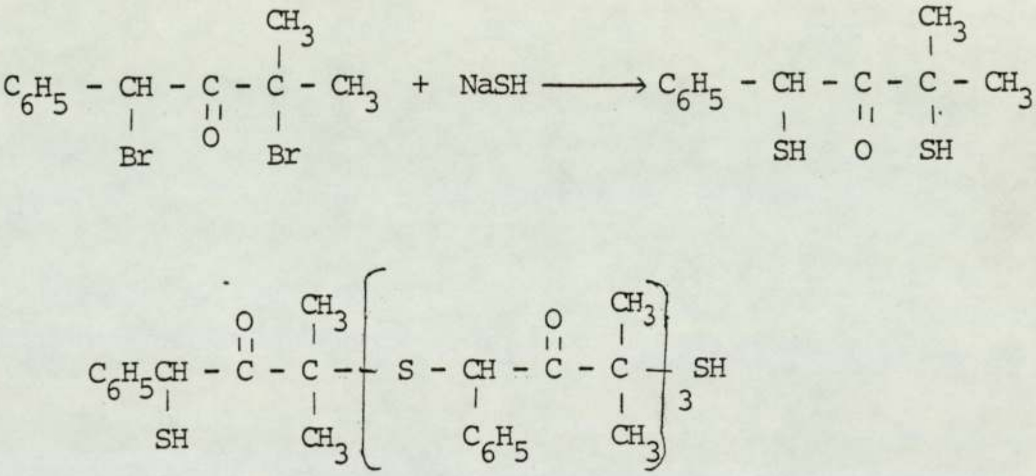
Photograph of a model of 2-chloro-4,4-dimethyl-2-phenylthietan-3-one.



5 - c : The reaction of a dibromoketone with sodium sulfide and sodium hydrosulfide.

5 - c - 1 : Dibromoketone with sodium hydrosulfide

The reaction of 1, 3-dibromo-3-methyl-1-phenylbutan-2-one with sodium hydrosulfide gave a mixture of the dithiols 79 and 80.



$$C_6H_5-\underset{Br}{\underset{|}{CH}}-\underset{O}{\underset{\|}{C}}-\underset{Br}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_3 + NaSH \longrightarrow C_6H_5-\underset{SH}{\underset{|}{CH}}-\underset{O}{\underset{\|}{C}}-\underset{SH}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_3$$

79

$$C_6H_5\underset{SH}{\underset{|}{CH}}-\overset{O}{\overset{\|}{C}}-\overset{CH_3}{\overset{|}{\underset{CH_3}{\underset{|}{C}}}}-\left[S-\underset{C_6H_5}{\underset{|}{CH}}-\overset{O}{\overset{\|}{C}}-\overset{CH_3}{\overset{|}{\underset{CH_3}{\underset{|}{C}}}}\right]_3-SH$$

80

The mixture was separated by vacuum distillation and two fractions were collected with boiling points of 82-88° and 90-98°/0.05mm/Hg. The fraction boiling at (82-88°) was found to be the dithiol 79 and the fraction boiling at (90-98°) was found to be the dithiol 80.

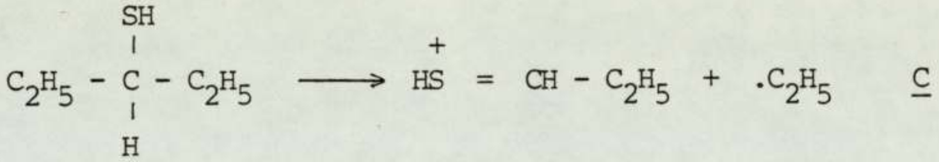
Analysis of first fraction :

The infrared spectrum showed peaks at 2560 and 1715cm^{-1} due to thiol (S - H) and carbonyl groups respectively. Proton nuclear magnetic resonance analysis showed that the chemical shift of the methine proton of the dithiol 79 had shifted to high field at $\delta = 3.8$ ppm when compared with the methine proton of the dibromoketone. The S - H proton appeared at $\delta = 3.15$ ppm. The relative intensity of the peak at 3.8 to the peak at

3.15 ppm is 1:2 which made it easy to differentiate between the methine and thiol proton. The mass spectrum of the dithiol 79 is expected to be similar to those of other thiols. Levy and Stahl(111) have studied the mass spectrum of thiol compounds. Fragmentation of these compounds gave ions A, B and C in high abundance.

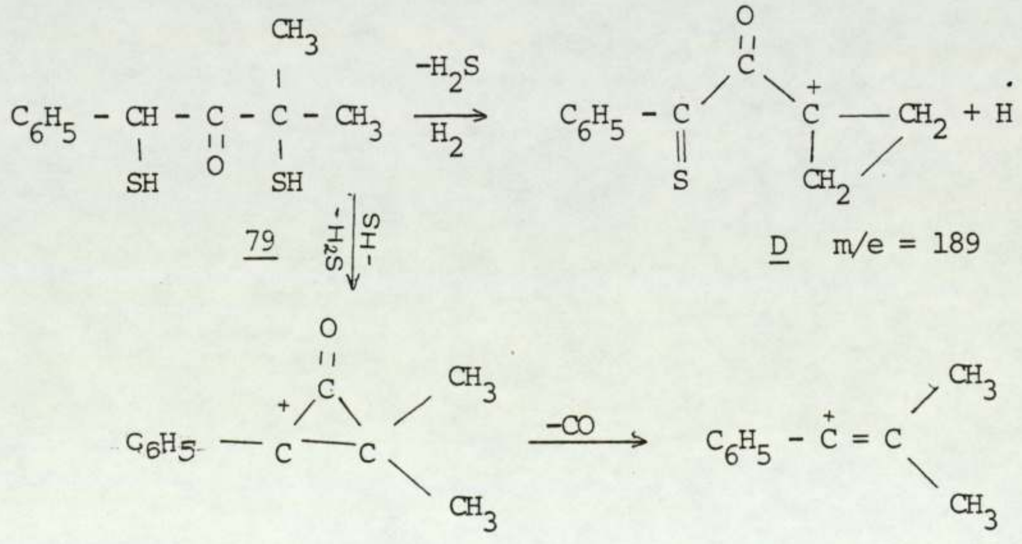
$$R - CH_2 - CH_2 - SH \longrightarrow CH_2 = \overset{+}{S}H + .CH_2R \qquad \underline{A}$$

$$R - CH_2 - CH_2 - SH \longrightarrow CH_2 = CH - \overset{+}{S}H_2 \ \ddot{+}\ R^{o} \qquad \underline{B}$$



$$C_2H_5 - \underset{H}{\overset{SH}{C}} - C_2H_5 \longrightarrow \overset{+}{HS} = CH - C_2H_5 + .C_2H_5 \qquad \underline{C}$$

Loss of hydrogen sulfide is another probable fragmentation mode in thiols(111). The mass spectrum of the dithiol 79 was found to be dissimilar to the general patterns of thiols. In this compound the major fragments are D, E and F. However, the dithiol 79 did not show a parent ion peak at 226 but the existence of fragments D, E and F suggested the formation of the dithiol 79 .



79

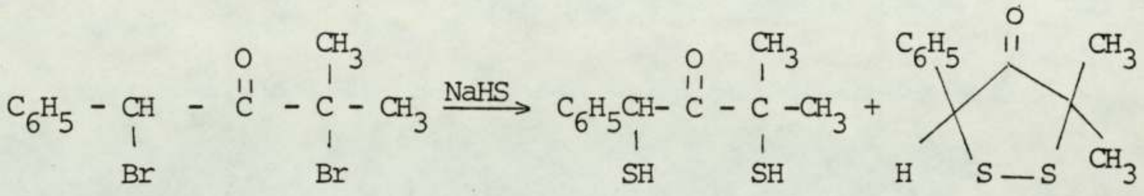
D m/e = 189

E m/e = 159

F m/e = 131

Analysis of the second fraction :

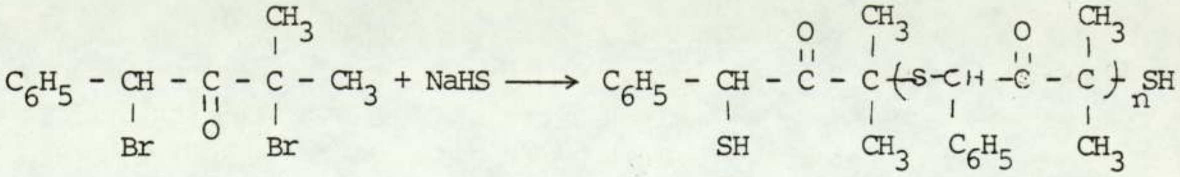
The infrared spectrum of this fraction showed peaks at 1715 and 2560 cm^{-1} due to the carbonyl and thiol groups respectively. The nuclear magnetic resonance spectrum showed two different methyl peaks at δ = 1.3 and 1.55 ppm, two different methine peaks at δ = 3.9 and 4 ppm and a phenyl ring at δ =7.25 ppm. At first sight this information suggests there is a mixture of dithiol 79 and dithiolanone 81,



79

81

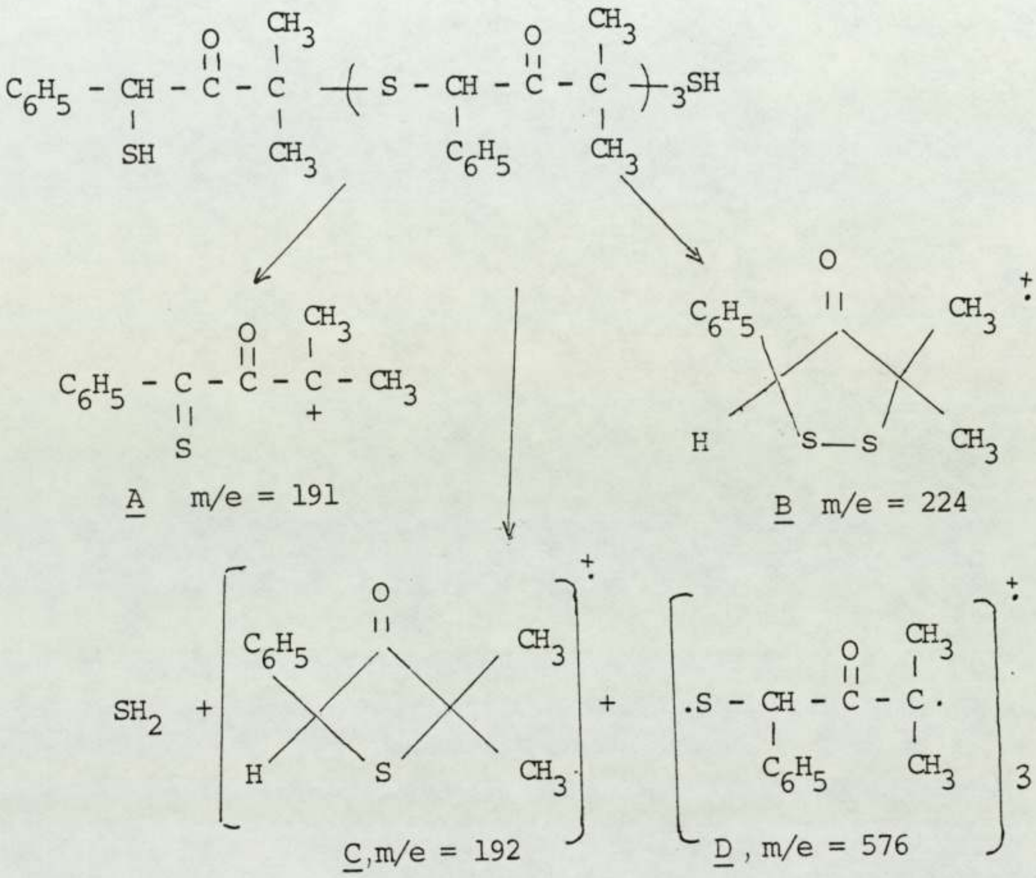
but further information suggested that this compound was in fact pure and is neither of these. The dithiolanone 81 was prepared by the reaction of a dibromoketone with sodium sulfide, the chemical shift of the methyl and methine protons of this compound was different to that shown in the nuclear magnetic spectrum of fraction 2, (see 5-c-2). The mass spectrum of fraction 2 gave an ion at $\frac{m}{e}$ 576 and the fragmentation patterns were different to those of the dithiol 79 and the dithiolanone 81. The high mass ion in the mass spectrum suggested polymerisation occurred during the reaction. The product therefore could be a polymer containing a thiol group, two different methine and methyl groups. This polymer might be the dithiol 80.



$$C_6H_5-\underset{Br}{CH}-\underset{O}{\overset{\|}{C}}-\underset{Br}{\overset{CH_3}{C}}-CH_3 + NaHS \longrightarrow C_6H_5-\underset{SH}{CH}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}\left(S-\underset{C_6H_5}{CH}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}\right)_n SH$$

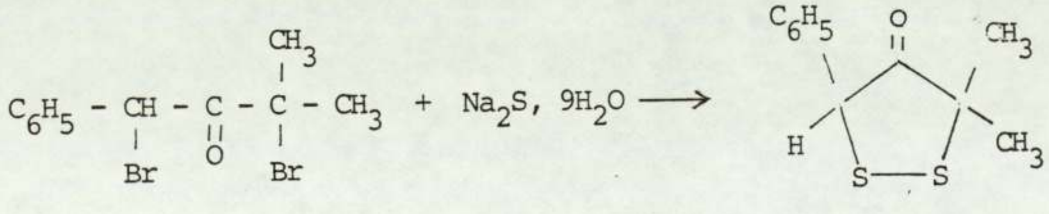
80 n = 3

The existence of ions at $\frac{m}{e}$ 576, 224, 192 and 191 in the mass spectrum is due to A, B, C and D.



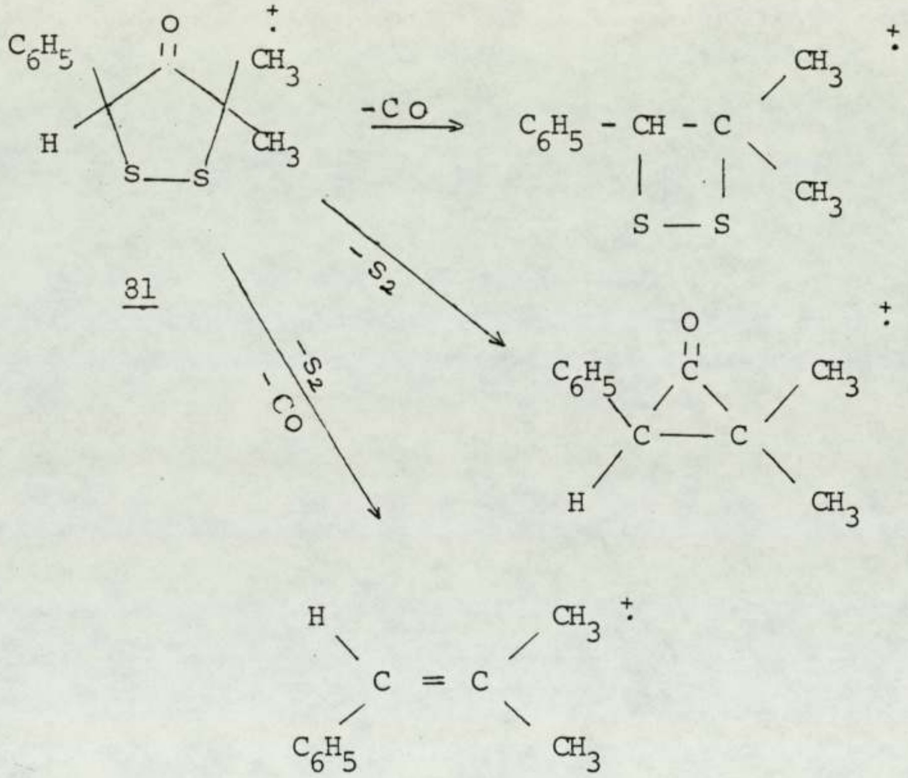
5 - c - 2 : Dibromoketone with Sodium Sulfide

1, 3-Dibromo-3-methyl-1-phenylbutan-2-one was treated with sodium sulfide. Analysis of the product suggested the presence of a mixture of the ketone, bromoketone and dithiolanone 81.



81

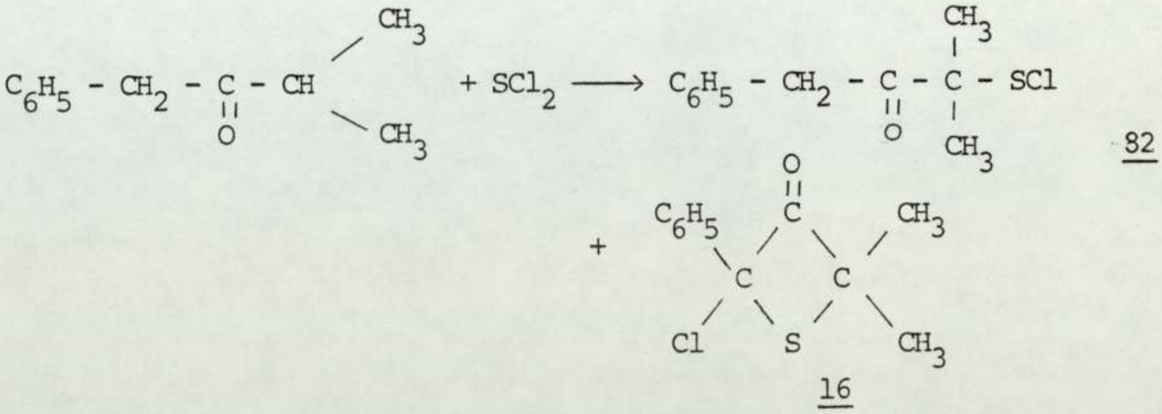
The carbonyl group of dithiolanone 81 gave a peak at 1725 cm^{-1} in the infrared spectrum. The two methyl groups in dithiolanone 81 have different chemical shifts at δ = 1.5 and 1.6 ppm in the nuclear magnetic resonance spectrum as expected. A single peak at δ = 4.7 ppm is due to methine proton. The mass spectrum of the dithiolanone 81 showed a parent ion at 224 mass units in high abundance. The ions M - S_2, M - CO and M - S_2 - CO were detected in the spectrum of the dithiolanone 81.



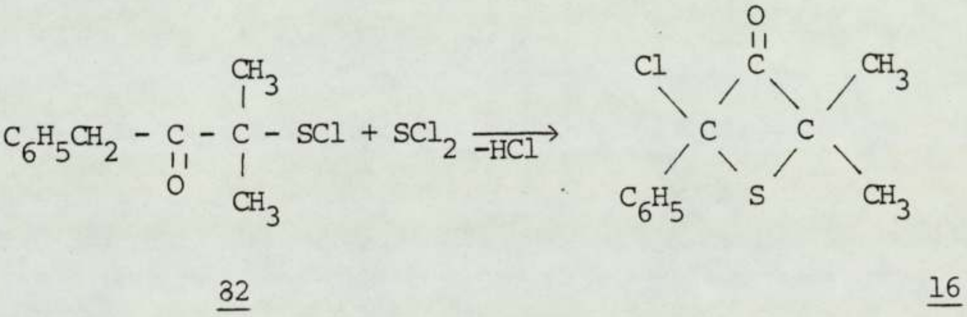
5 - d : <u>Preparation of the β-ketosulfenyl chlorides</u>

Several conditions have been used for the preparation of 3-chlorosulfenyl -3-methyl-1-phenylbutan-2-one.

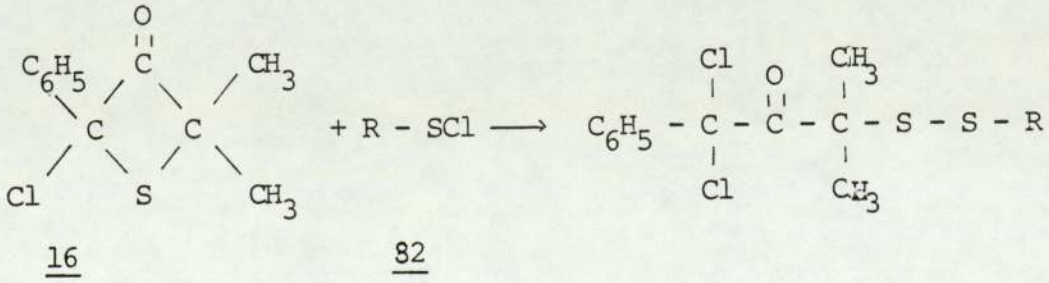
I : The treatment of one equivalent of benzyl isopropyl ketone in carbon tetrachloride with sulfur dichloride at room temperature probably gave a mixture of starting material, the sulfenyl chloride 82 and the thietanone 16.

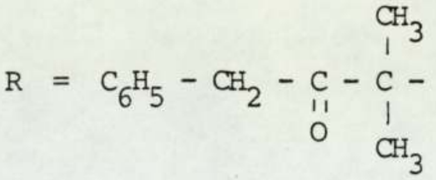


In this reaction the rate of cyclization is slower than the rate of formation of sulfenyl chloride.



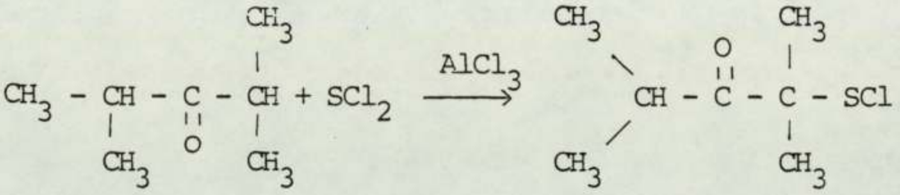
The position of the carbonyl group of the thietanone 16 and the sulfenyl chloride 82 were at 1780 and 1710cm^{-1} respectively. The separation of the mixture is not possible by distillation. This could be due to reaction of the thietanone 16 with the sulfenyl chloride 82 .





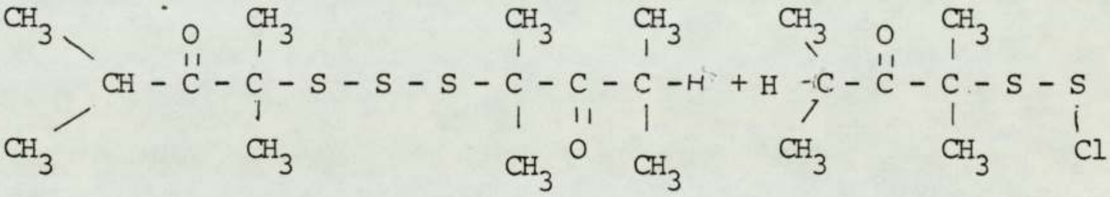
$R = C_6H_5-CH_2-\overset{O}{\overset{\|}{C}}-C(CH_3)_2-$

II : Harris and feisst(112) have prepared the sunfenyl chloride 83 in low yield by treating di-isopropyl ketone with sulfur dichloride in the presence of aluminium chloride.



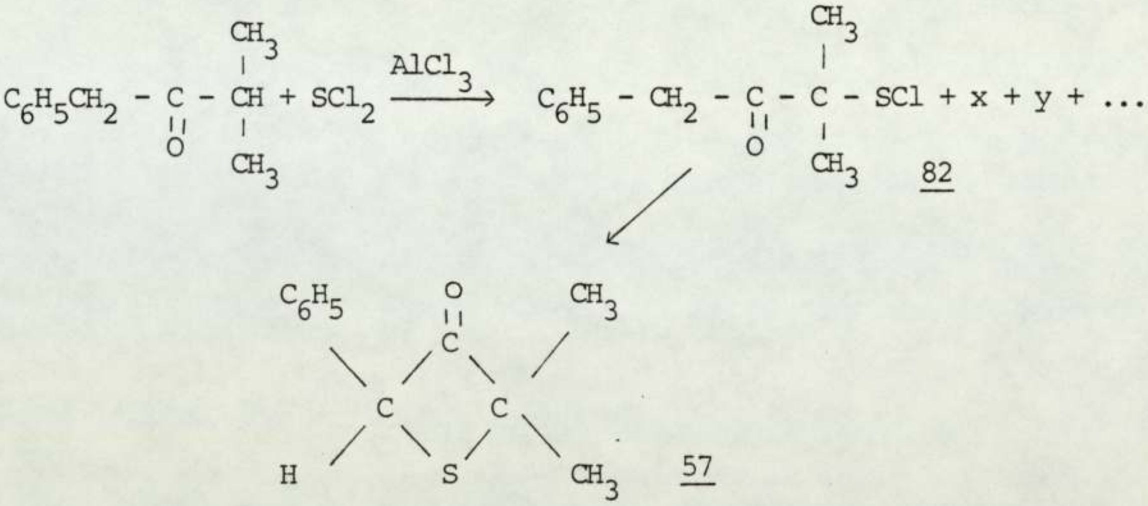
$CH_3-CH(CH_3)-\overset{O}{\overset{\|}{C}}-CH(CH_3)-CH_3 + SCl_2 \xrightarrow{AlCl_3} (CH_3)_2CH-\overset{O}{\overset{\|}{C}}-C(CH_3)_2-SCl$

83



$(CH_3)_2CH-\overset{O}{\overset{\|}{C}}-C(CH_3)_2-S-S-S-C(CH_3)_2-\overset{O}{\overset{\|}{C}}-C(CH_3)_2-H + H-C(CH_3)_2-\overset{O}{\overset{\|}{C}}-C(CH_3)_2-S-S-Cl$

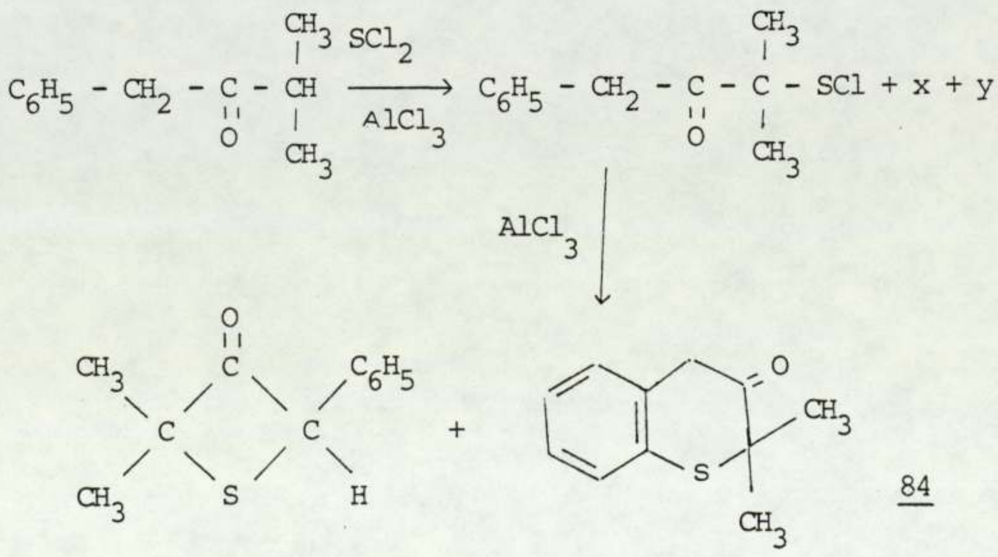
The same conditions were used for the preparation of the sulfenyl chloride 82. This reaction gave several compounds. Analysis of one of the fractions showed the presence of a mixture of thietanone 57 and the sulfenyl choride 82. The formation of the thietanone 57 was found after distillation. In fact some of the sulfenyl chloride 82 changed to thietanone 57 during the distillation.



82

57

The carbonyl absorption of thietanone 57 is at 1765 cm^{-1}, in the infrared spectrum. The single peaks at δ = 1.5, 1.8 and 3.95 ppm are due to the two methyls and methine protons. The single peak at δ = 1.5 ppm could be due to two methyl groups in the sulfenyl chloride and these have the same shift as one of the methyl groups of the thietanone 57. The peak at δ = 3.85 ppm was probably due to the methylene protons of the sulfenyl chloride 82. The reaction of benzyl isopropyl ketone with sulfur dichloride in the presence of aluminium chloride could also give a thiacyclic compound 84.



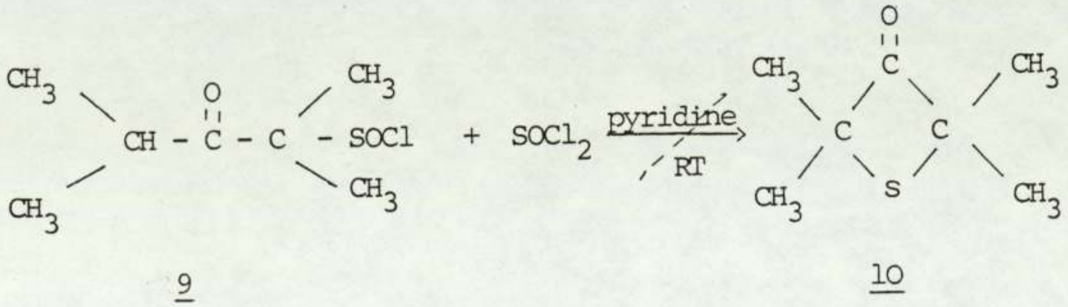
84

We tried to increase the amount of the sulfenyl chloride 82 and decrease the side reactions by using pyridine as a catalyst. However, by using a small amount of pyridine the reaction gave the sulfenyl chloride 82, but the product decomposed under distillation. The nuclear magnetic spectrum of the crude product showed peaks at $\delta = 1.4$, 3.85 and 7.2 ppm due to six methyl protons, two methylene and five phenyl protons. These peaks confirmed the existence of the sulfenyl chloride 82 in the mixture.

5 - e : The reactions of the sulfinyl chlorides.

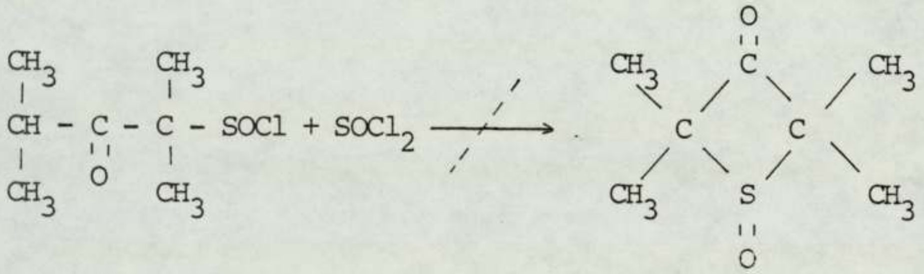
5 - e - 1 : 2-Chlorosulfinyl-2, 4-dimethylpentan-3-one.

The reaction of the sulfinyl chloride 9 with thionyl chloride in the presence of aluminium chloride was studied by Pizey et al.(36). They found the sulfinyl chloride 9 did not react with thionyl chloride under this condition. Non-reactivity was rationalized(36) in terms of non-formation of the enol form. The nuclear magnetic resonance spectrum of the sulfinyl chloride 9 showed it to exist as the keto rather than the enol form. For further investigation the di-isopropyl ketone was treated with excess sulfuryl chloride and only the monosubstituted product was formed(36). Gupta(21) reported that the sulfinyl chloride 9 with thionyl chloride in the presence of pyridine at room temperature gave the thietanone 10.



However when the same reaction was done under similar conditions the resulting compound was found not to be the thietanone 10.
In the infrared spectrum there was not a carbonyl group at 1765cm^{-1} as expected for structure 10. The position of the carbonyl group of the resulting compound was similar to that of the starting material. When the reaction mixture was refluxed for four days in the presence of pyridine, the infrared spectrum showed the presence of a carbonyl group in a five membered ring. The proton nuclear magnetic resonance spectrum showed four singlet peaks. The product was distilled under vacuum and the fraction boiling at 84-86°/4mmHg was collected.

Treatment of the sulfinyl chloride 9 with thionyl chloride was expected to give thietanone 1-oxide 85.

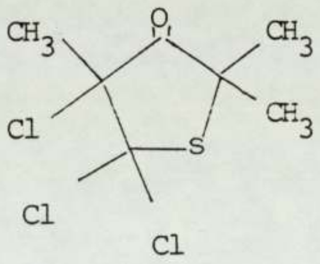


9 85

The thietanone 1-oxide 85 (113, 114) has been reported to be a white solid with a melting point of 106° having carbonyl and sulfoxide infrared absorbances at 1705 and 1070cm^{-1} respectively. Furthermore the methyl protons of the thietanone 1-oxide 85 gave singlets at δ = 1.6 and 1.5 ppm(113, 114).

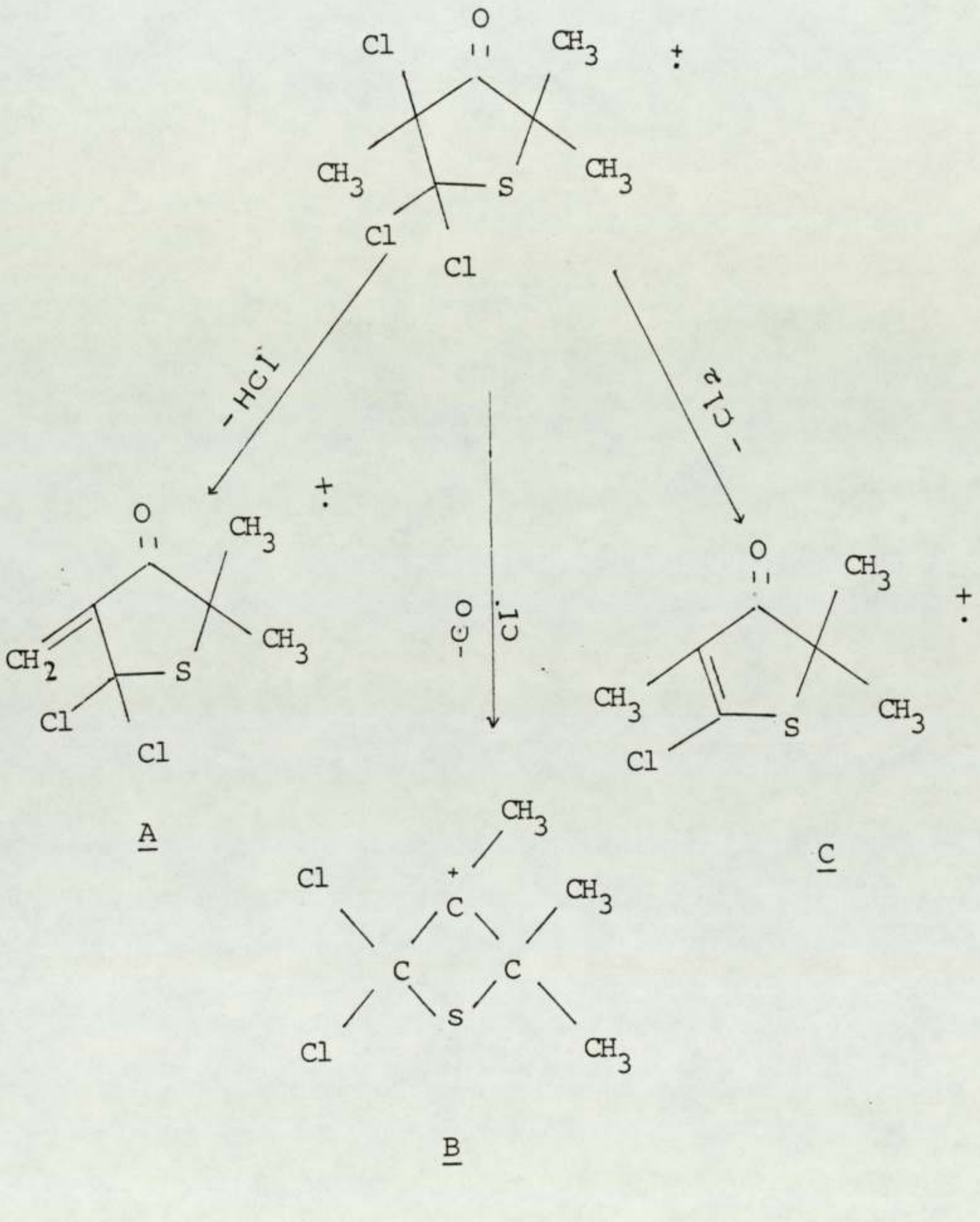
However for the fraction that boiled at 84-86°/4mm/Hg in our reaction the spectroscopy data found did not correspond with that described for the thietanone 1-oxide 85.

The infrared spectrum of the product showed strong peaks at 1750 and 1070cm^{-1} and the nuclear magnetic resonance spectrum showed peaks at δ = 1.6, 1.8 and 1.95 ppm. The mass spectrum showed a parent ion peak at 246 mass units. The accurate mass spectrum gave the molecular formula $C_7H_9Cl_3OS$ for the ion at m/e246. The relative intensity of the peaks at 246, 248, 250 and 252 was 100:99:33:1, which confirmed the existence of three chlorine atoms in the molecule. None of the fragment patterns in the mass spectrum showed the existence of sulfur monoxide (S = O) group. A peak due to sulfur monoxide was not found at 48 mass units. If the bands at 1750 and 1070 cm^{-1} are due to carbonyl and sulfoxide groups in the infrared spectrum the molecular formula should have two oxygen atoms, hence a band at 1070cm^{-1} in the infrared spectrum does not belong to the sulfoxide functional group (S = O). The possible structure of fraction 2 is the thiolanone 86.

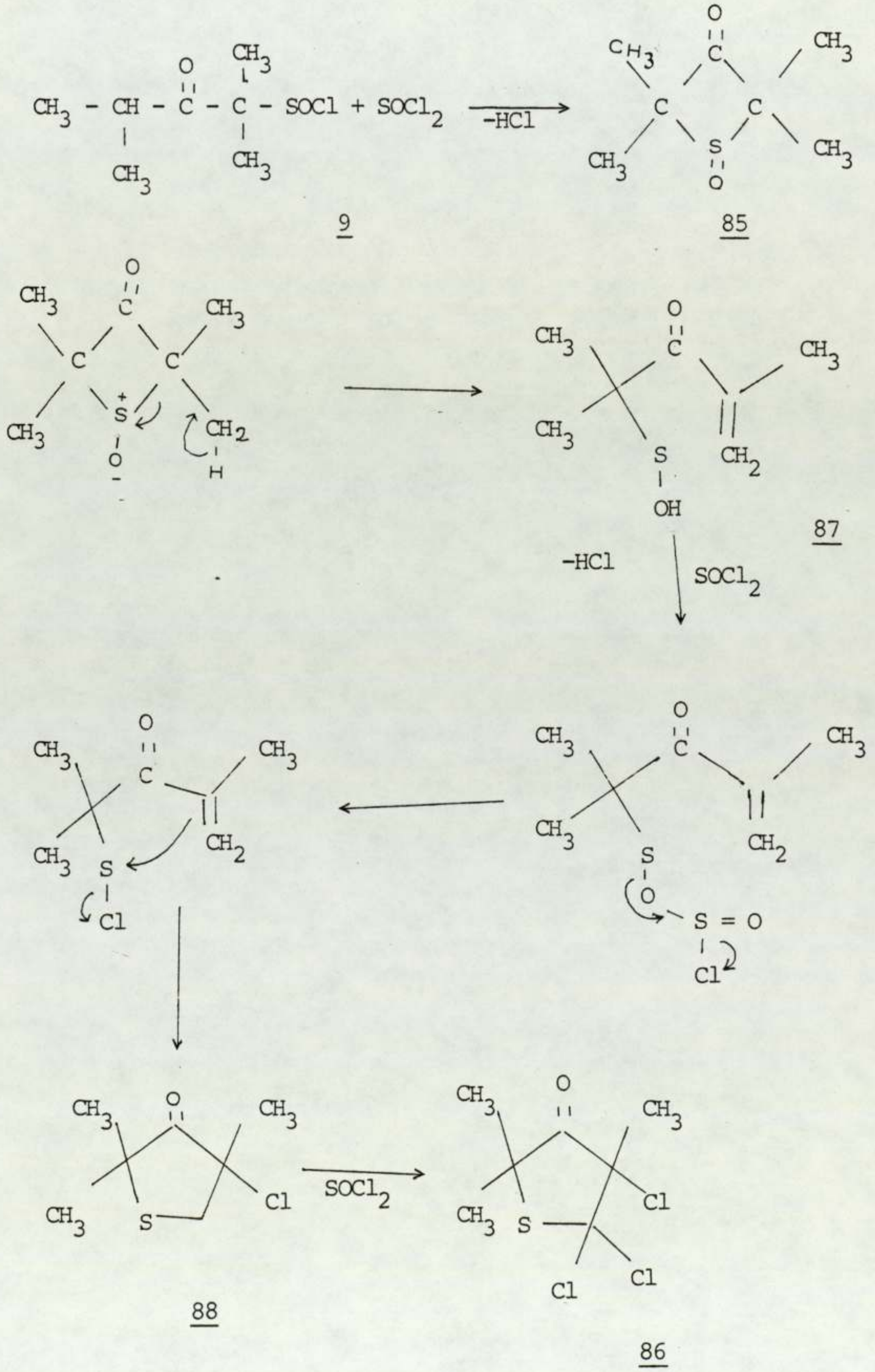


86

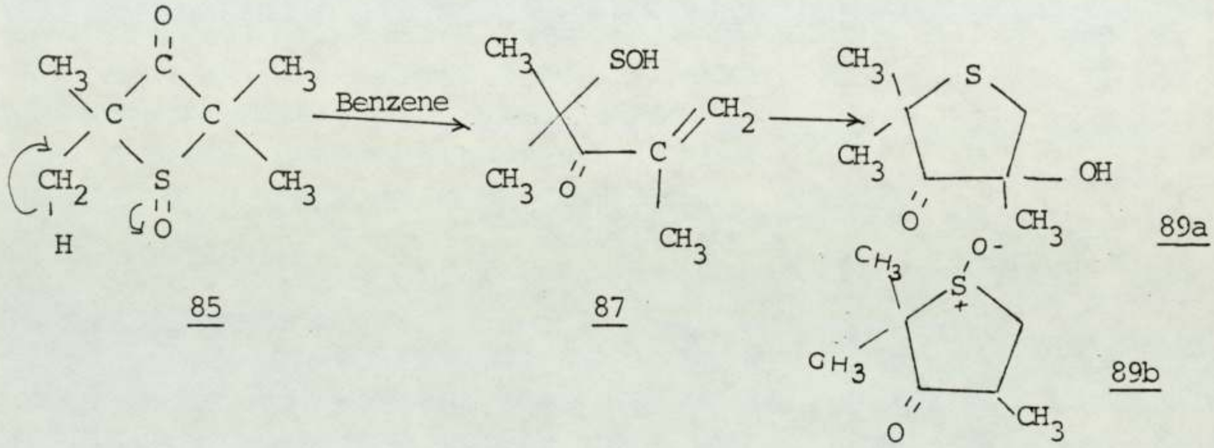
The major fragments in the mass spectrum are due to loss of HCl, (CO + Cl) and chlorine.


-HCl
-CO
Cl
-Cl2
A
B
C

The formation of the thiolanone 86 is presumably via the route shown.

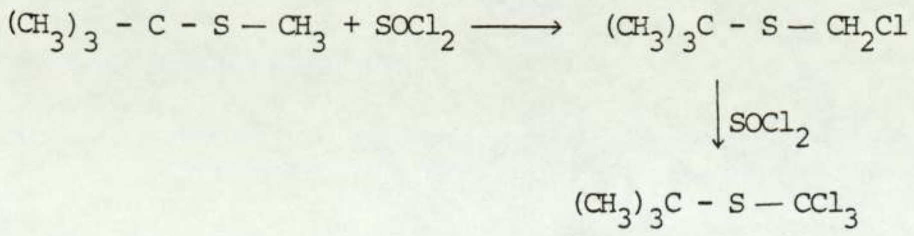


Bushby(114) discovered the sulfoxide 85 is thermally unstable and undergoes rearrangements very similar to those of the penicillin S-oxides(115). In this case the intermediate sulfenic acid 87 cyclizes both in the RSO + H and in the RS +OH sense, and both reactions involve ring expansion. When the sulfoxide 85 is heated in refluxing benzene, the resulting materials were 89a and 89b.



85 87 89a 89b

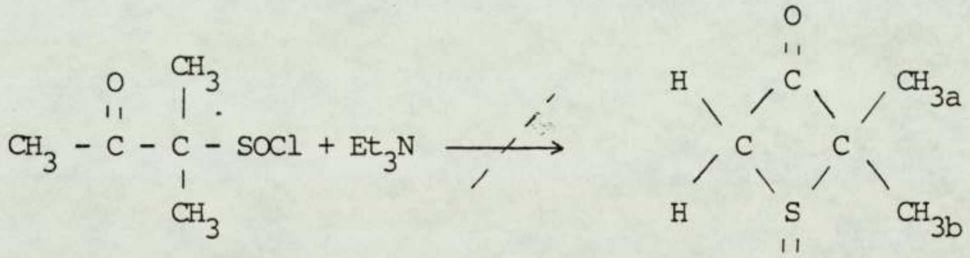
On these grounds it is possible the treatment of the sulfinyl chloride 9 with thionyl chloride gave the thietanone 1-oxide 85. The thietanone 1-oxide 85 is unstable and undergoes ring opening to the sulfenic acid 87. The intermediate sulfenic acid 87 cyclizes to the thiolanone 88. The chlorination of the monochlorothiolanone 88 is possible by thionyl chloride to give the trichlorothiolanone 86. However thionyl chloride is not usually a chlorinating agent for methylene protons, but it is able to chlorinate methyl protons attached to sulfur atom e.g. tert-butyl methyl sulfide with thionyl chloride gives tert-butyl trichloromethyl sulfide(116).



$$\begin{aligned}(CH_3)_3-C-S-CH_3 + SOCl_2 &\longrightarrow (CH_3)_3C-S-CH_2Cl\\ &\qquad\big\downarrow SOCl_2\\ &\qquad (CH_3)_3C-S-CCl_3\end{aligned}$$

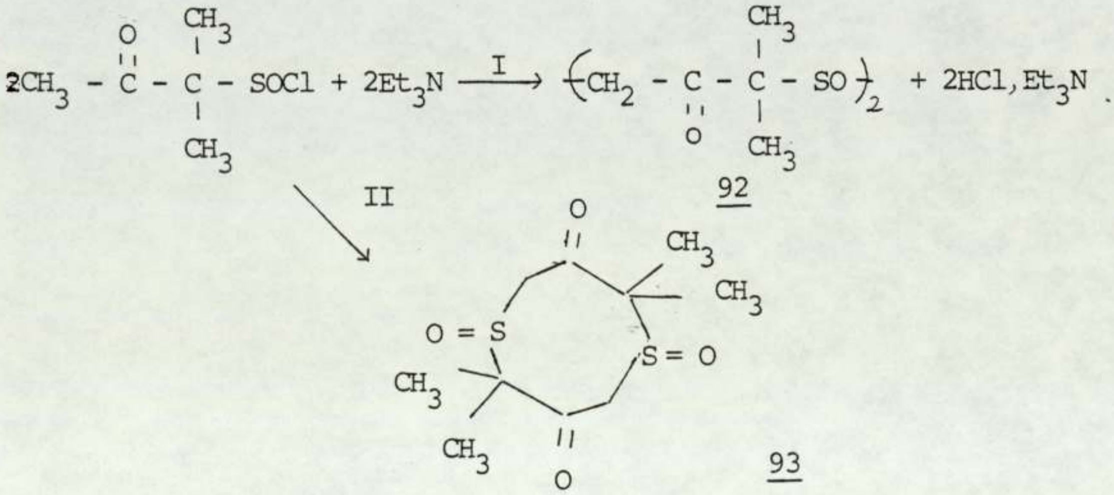
5 - e - 2 : 3-Chlorosulfinyl-3-methylbutan-2-one

The synthesis of the thietan 1-oxide was attempted by treating the sulfinyl chloride 90 with triethylamine. Treatment of one equivalent of the sulfinyl chloride with one equivalent of triethylamine gave one equivalent of triethylamine hydrochloride, however the thietanone 1-oxide 91 was not found (Infrared spectrum analysis show no high field carbonyl group at 1780cm^{-1})nuclear magnetic resonance spectrum analysis did not show peaks for methyl protons (a, b) at 1.5, 1.6 ppm and methylene protons at δ = 4-4.7 ppm in a relative intensity of 6:2. The elimination of one proton is expected from the methyl protons in the α-position to the carbonyl group.

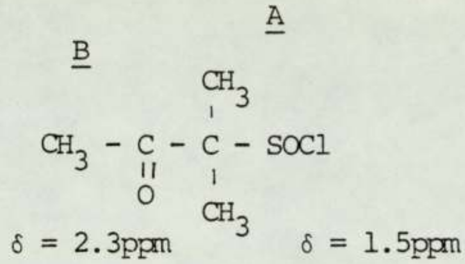


90 91

The thietanone 1-oxide 91 may not have formed because of dimerization of the reaction intermediate to give either structure 92 or 93 .



The spectroscopy data however, reject the formation of these structures as well. The infrared spectrum of the product showed peaks at 1690, 1260, 1145 and 1070cm^{-1}. The peak at 1690cm^{-1} is probably due to a carbonyl group. The absorption frequencies of the sulfoxide group (S = O) could be at 1070 and 1145cm^{-1}. The nuclear magnetic resonance spectrum of the product gave peaks at δ = 1.5 , 2.3 and 7.5 ppm in a relative intensity of 12:3:1 respectively. The peaks at δ = 1.5 and 2.3 ppm of the product are in the same position as in the starting material (the sulfinyl chloride 90).

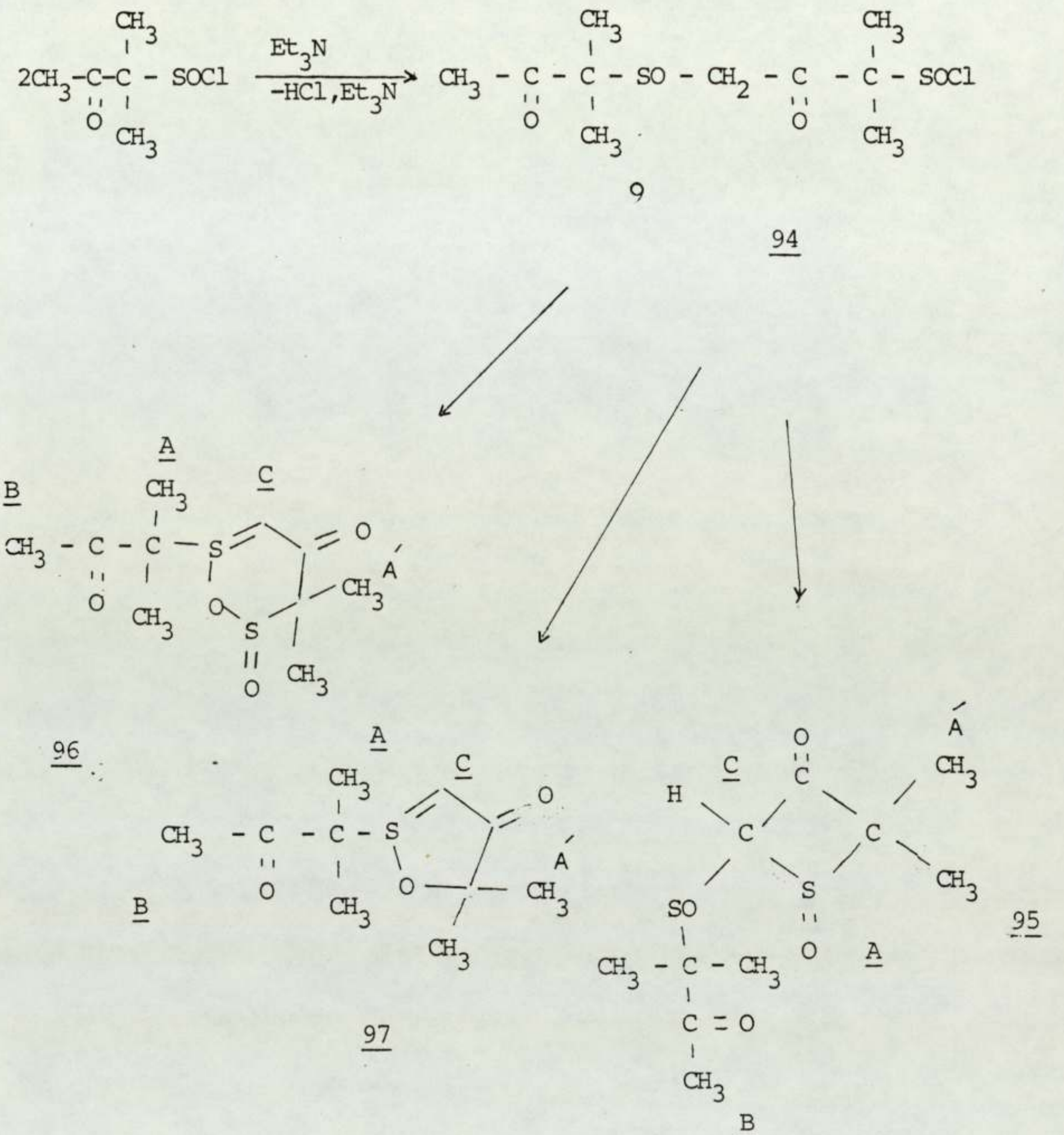


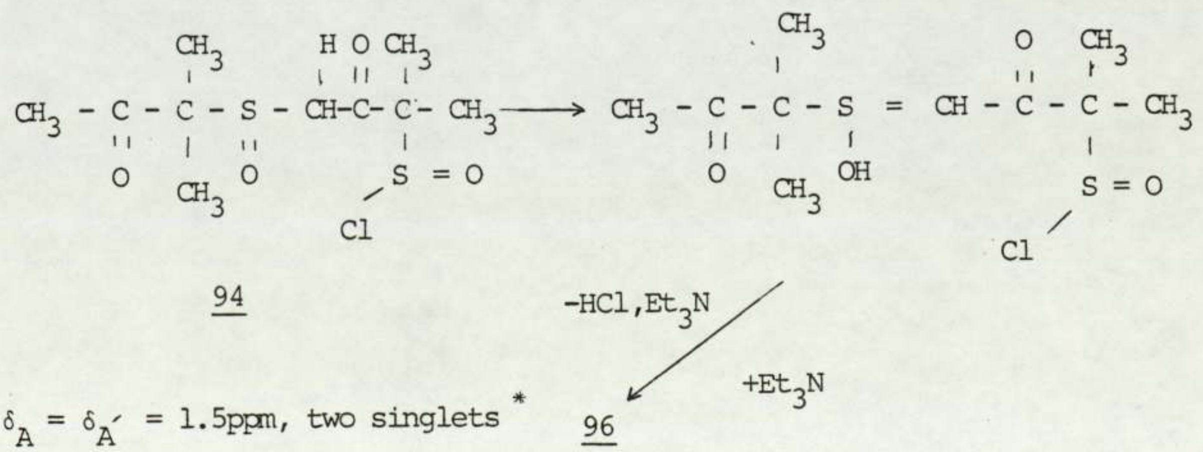
$CH_3-C(=O)-C(CH_3)_2-SOCl$

90

From the integral of the spectrum of the product of the reaction and from a comparison of the chemical shift of the methyl groups of the sulfinyl chloride 90 with those of the product, it was found that there was one methyl group in position B and four methyl groups in position A and the peak at δ = 7.5 ppm was due to a methine joined to a carbonyl group. The nuclear magnetic resonance and infrared spectra lead us therefore to suggest scheme a for this reaction (described below).

a : In the first stage loss of proton from methyl B.
The methylene protons of the compound 94 are more acidic than the other protons so the methylene group can probably lose a proton in the second stage.





$\delta_A = \delta_{A'}$ = 1.5ppm, two singlets*

δ_B = 2.3 ppm, one singlet

δ_C = 7.5 ppm, one singlet

* :See p. 65

The absence of a carbonyl group at approximately 1760 - 1790 cm^{-1} in the infrared spectrum contradicts structure 95. However the nuclear magnetic resonance and infrared spectrum of the product are correct for compound 96 but the C, H, S analysis of the product showed a molecular formula $C_{10}H_{16}O_3S$. The mass spectrum gave a parent ion peak at 298 mass units. The molecular formula of this ion was $C_{10}H_{18}O_2S_4$ which is different from that suggested by elemental analysis.

Compound 97 agreed with the nuclear magnetic resonance and infrared spectra and C, H, S analysis.

CHAPTER 6

THE REACTIONS OF THIETAN-3-ONES

Page

CHAPTER 6

Introduction

* 2-Chloro-4,4-dimethyl-2-phenylthietan-3-one.

CHAPTER SIX

6: The reactions of thietanones.

6 - a: The nucleophilic reactions of thietanones.

INTRODUCTION

In recent years a new view of aliphatic substitutions has been proposed.(117, 118) Sneen (117) has contended that, in most, if not all cases of substitution by an added nucleophile, nucleophilic attack does not take place until the substrate has ionized, without nucleophilic assistance, to at least the intimate ion-pair stage (eq.1)

$$RX \underset{K_{-1}}{\overset{K_1}{\rightleftharpoons}} R^+ X^- \xrightarrow{K_2(\bar{N})} NR + X^- \qquad (1)$$

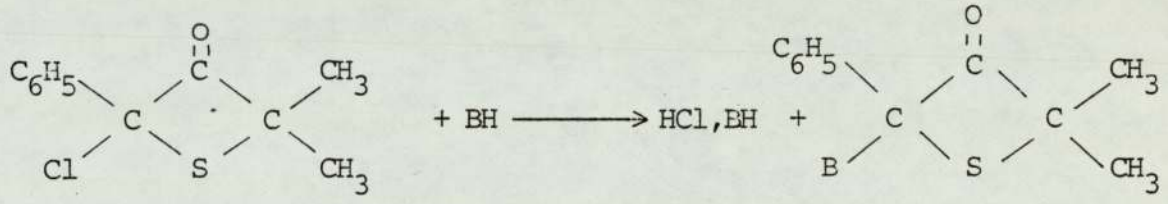
The nucleophile is presumably thought to be more strongly attracted to the cationic carbon than the neutral carbon in RX, and so performs the act of substitution by anion interchange at the ion-pair stage. When $[\bar{N}_o] \gg [RX]_o$, the steady-state rate equation for K_{obsd}, the pseudo-first-order rate constant, is given by

$$K_{obsd} = \frac{K_1K_2[\bar{N}]}{K_{-1} + K_2[\bar{N}]} \qquad (2)$$

There are two limiting cases: I: $K_2[\bar{N}] \gg K_{-1}$, so $K_{obsd} = K_1$ and we have rates independent of $[\bar{N}]$ and SN_1-like process; II: $K_{-1} \gg K_2[\bar{N}]$, $K_{obsd} = K_1K_2[\bar{N}]/K_{-1}$ so that the reaction is first order in $[\bar{N}]$ and second order overall. These two cases corresponding respectively to rate-limiting ionization and nucleophilic attack on a preformed ion pair, are thus kinetically indistinguishable from SN_1 in the former limit and the traditional SN_2 in the latter. If, however, $K_{-1} \simeq K_2 [\bar{N}]$, eq (2) shows that the order with respect to $[\bar{N}]$ is between first and second, so that this is a hypothetical borderline region.

6 - a - 1: Aminothietanones .

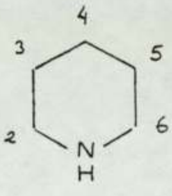
The treatment of one equivalent of the 2-chlorothietanone 16 with two equivalents of the amine (Piperidine, Morpholine or Pyrrolidine) gave the thietanone 98



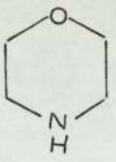
16

98

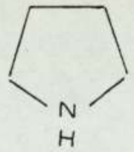
98	BH
A	Piperidine
B	Morpholine
C	Pyrrolidine



A



B

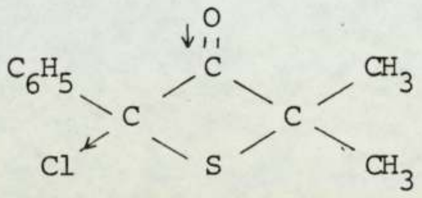


C

Analysis of 98A

The infrared spectrum of the piperidinothietanone 98A showed a strong absorption band at 1760cm^{-1}. The carbonyl absorption of 98A is shifted by about 20cm^{-1} to a lower wave-number when compared with the absorption of the carbonyl group of the 2-chlorothietanone 16. The electron

withdrawing and strain effect in the 2—chlorothietanone 16 raises the carbonyl frequency to 1780cm^{-1} (see page 124).
However, in the aminothietanone 98 there is still strain, but electron donation lowers the carbonyl stretch frequency to 1760cm^{-1}. On the other hand the inductive effect of amino groups is less than that of a chlorine atom.



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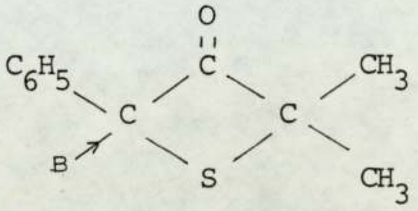
strain and electron withdrawing effect



98

strain effect

The appearance of new peaks at 1035 and 1230cms^{-1} might be due to a carbon-nitrogen single bond stretching frequency in the infrared spectrum. The nuclear magnetic resonance spectrum showed two single peaks at δ = 1.35, 1.6ppm due to two methyl groups, a broad singlet peak at δ = 2.5 ppm due to methylene protons (2,6). The chemical shift of methylene protons (3,4,5) are at the same field as the methyl protons, δ = 1.35-1.8ppm. The relative intensity of peaks at δ = 1.35 - 1.8 ppm to the peak at δ = 2.5ppm is 12:4 which was correct for protons in structure 98A.

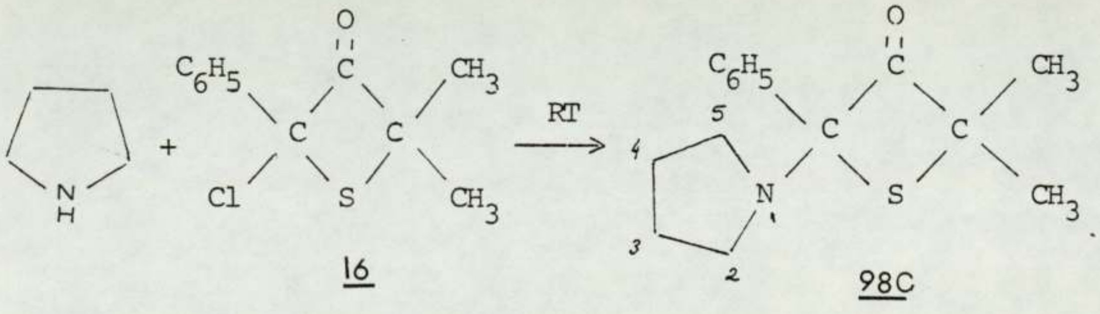
The accurate mass spectrum of an ion at $\frac{m}{e}$275 gave the molecular formula as $C_{16}H_{21}NOS$ and elemental analysis confirmed this molecular formula.

Analysis of the morpholinothietanone 98B.

The carbonyl absorption frequency of the morpholinothietanone 98B is at 1755 cm^{-1} in the infrared spectrum. The two methyl protons of 98B have different chemical shifts at $\delta = 1.3$ and 1.5 ppm as expected. The methylene protons gave two triplets at $\delta = 2.3$ and 3.6 ppm in the nuclear magnetic resonance spectrum. The mass spectrum showed a parent ion peak at 277 mass units. The accurate mass spectrum of an ion at $\frac{m}{e}$ 277 gave the molecular formula as $C_{15}H_{19}NO_2S$. The molecular formula $C_{15}H_{19}NO_2S$ was also obtained by elemental analysis.

Analysis of 98C.

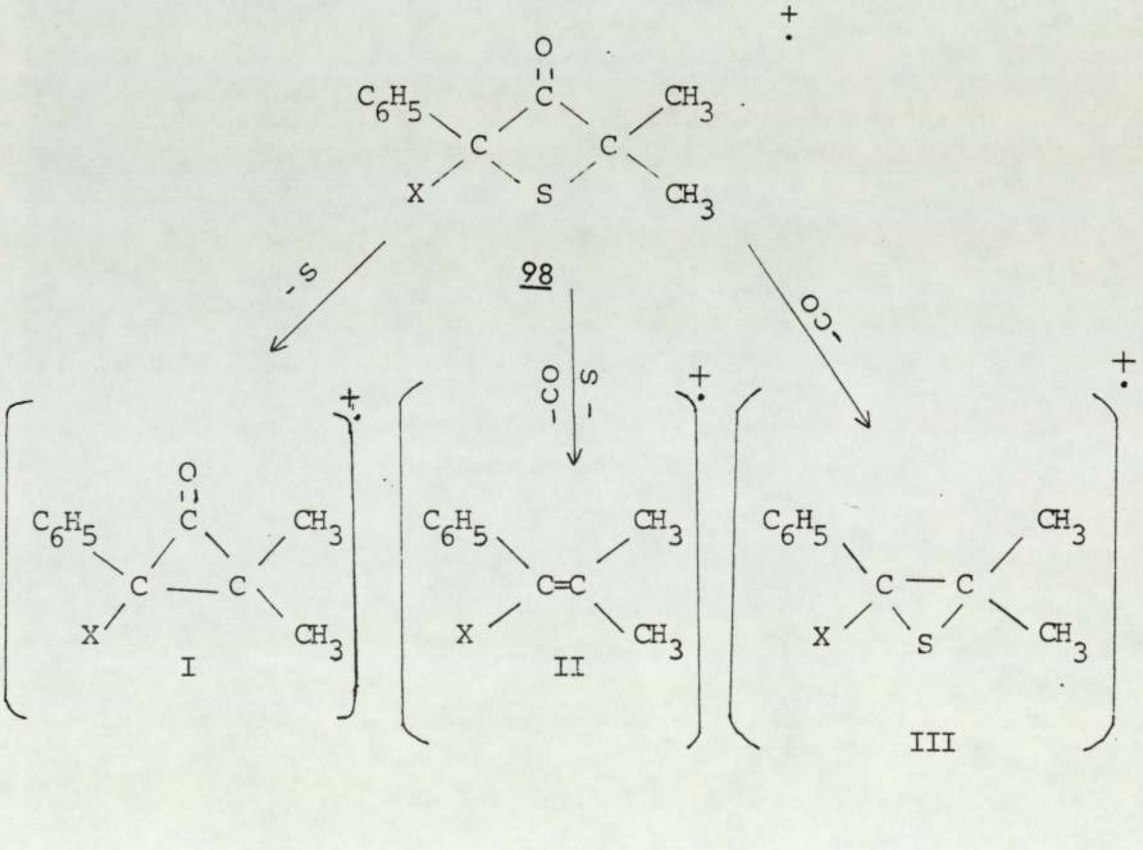
This reaction proceeds similarly to those in which piperidine and morpholine are nucleophiles. However the product is not as stable. Heating causes cleavage of the C-S bond and decomposition.



The infrared spectrum showed peaks at 1760cm^{-1} and 1020cm^{-1} due to the carbonyl and C-N bonds respectively.

The nuclear magnetic resonance spectrum showed a multiplet at $\delta = 2.6$ppm due to the methylene protons 2 and 5. The methylene protons 3 and 4 are at the same field strength as the methyl protons. For this reason, the two single peaks of the methyl protons are slightly deformed. The mass spectrum of the thietanone 98C showed a molecular ion peak at 261 mass units. The accurate mass spectrum of an ion at $\frac{m}{e}$ 261 gave the molecular formula as $C_{15}H_{19}NOS$.

The mass spectra of the thietanones 98A, 98B and 98C exhibit a detectable parent ion but the most abundant ions in the spectrum are mass ions M-32, M-28 and M-60. The most important fragmentation pathway involves the loss of a sulfur atom to form I, followed by loss of carbon monoxide to form II. The fragment III is also found.

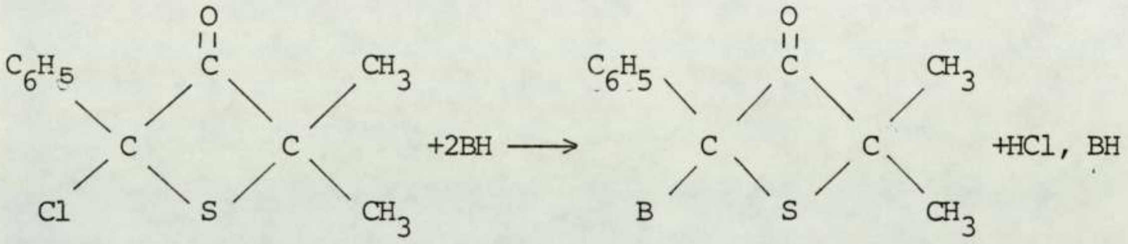


X = Piperidine, Morpholine, Pyrrolidine

6 - a - 2: A study of the reaction pathway of the thietanone with amines.

It was of interest to study the reaction of a thietanone with amines. The amines used were piperidine, morpholine and pyrrolidene.

The reaction was found to proceed with replacement of the chlorine atom in the thietanone by the amino group.



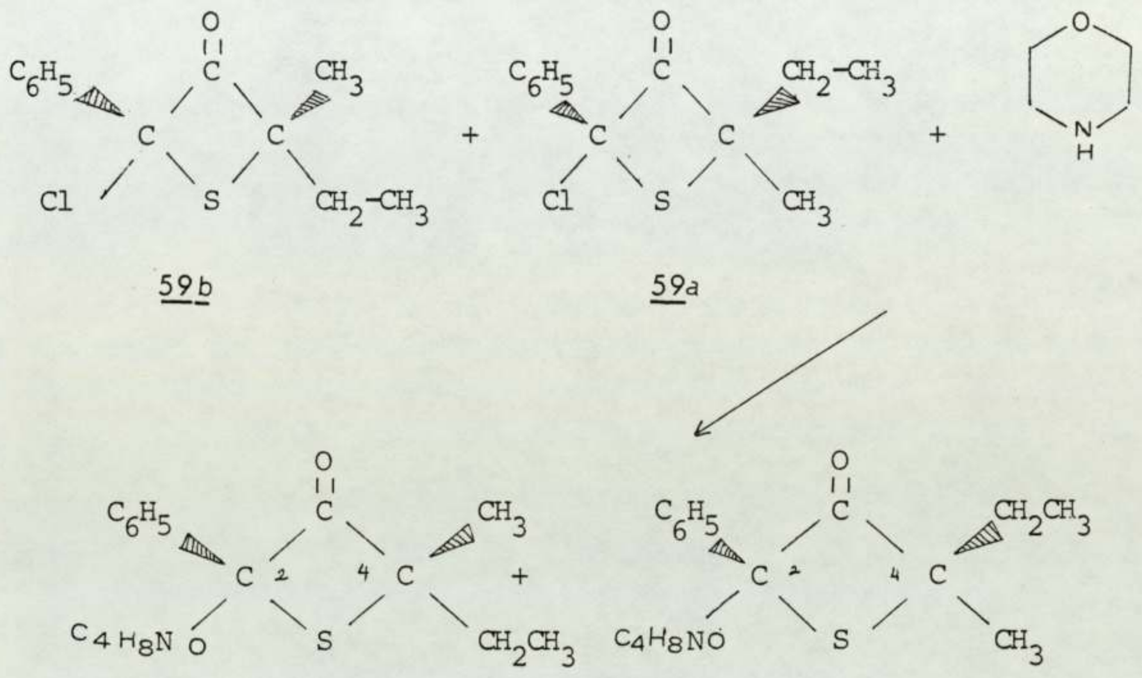
16.   98

BH = Piperidine, Morpholine and Pyrrolidine.

The rate of the reaction was found to increase in the order piperidine < morpholine. The PK_a values of piperidine and morpholine are 18.92 and 16.61 respectively.(119, 120)
Thus it is apparent that the rate of the reaction is not in accordance with basicity. If the reaction were in accordance with basicity or nucleophilicity then the pathway would be substitution nucleophilic (SN) (see page 191). Another pathway for the reaction would be by ring opening of the C-S bond followed by ring closure.

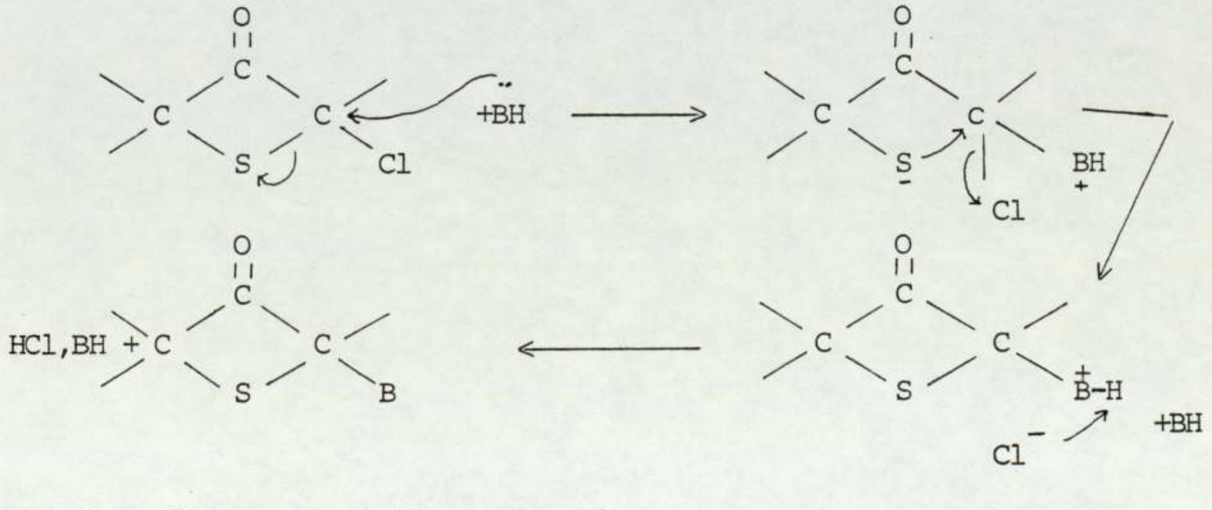
In order to test this suggestion, the following experiment was carried out. A 1:1 mixture of the cis- and trans-isomer of the chloro(ethyl) thietanone 59 was treated with morpholine and the product was studied by nuclear magnetic resonance spectroscopy.

The product was found to be an unequal mixture of two product isomers. Nuclear magnetic resonance spectroscopy is a useful technique for the measurement of the relative abundance of the two isomers because of the facile measurement of protons on the groups at the 4-position



59b 59a

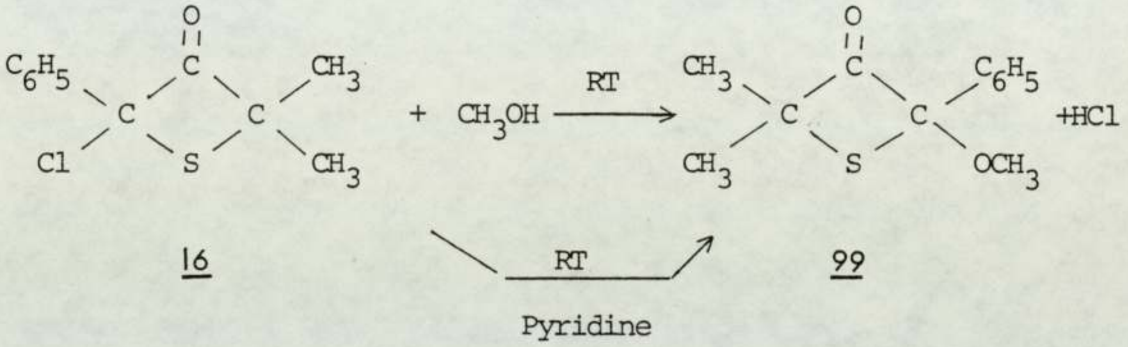
If the reaction proceeded by nucleophilic substitution type pathway, equal quantities of both isomer would have been expected. However, if ring opening were to occur, then before ring closure, a certain amount of bond rotation could occur, therefore giving rise to unequal isomer ratios. This is in fact what was observed. Hence the reaction pathway might proceed via ring cleavage -



BH = Pyrrolidine, morpholine, piperidine.

6 - a - 3: The Methoxythietanone.

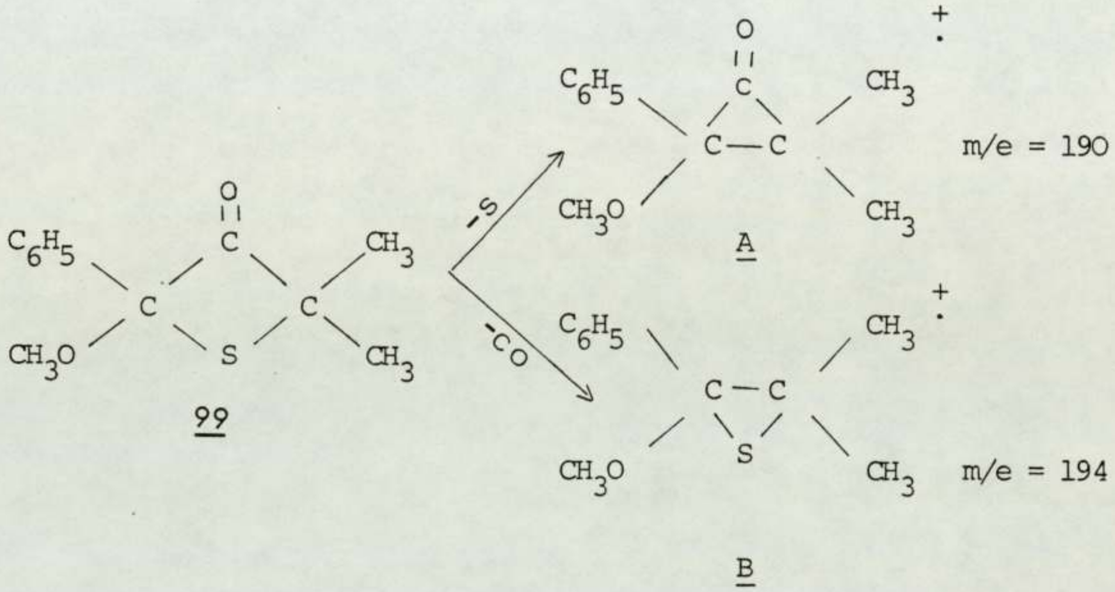
The treatment of the 2-chlorothietanone 16 with excess of dry methanol at room temperature gave the methoxythietanone 99 in low yield. When the reaction was carried out in the presence of a small amount of pyridine as a catalyst, the percentage of the product increased. Pyridine causes the forward reaction to shift to the right.



The position of carbonyl group of the methoxythietanone 99 is at 1770cm^{-1} and the C-H stretch of the methyl and phenyl groups in the thietanones 16, 98, 99 has characteristic absorptions at approximately 3060-2860cm^{-1} in the infrared spectrum. These peaks are usually weak or medium in strength. The C-H bending vibration for the methoxyl group of the thietanone 99 is at 2820cm^{-1} in the infrared spectrum. The nuclear magnetic resonance spectrum of the product showed peaks at δ = 1.4, 1.7 3.4 and 7.45ppm in a relative intensity of 3:3:3:5.
The appearance of a new peak (at δ = 3.4ppm) in the spectrum of the product is due to the methoxyl group.

The methoxy-compounds usually lose a methoxyl group to give the ion ($M-OCH_3$) in the mass spectrum.

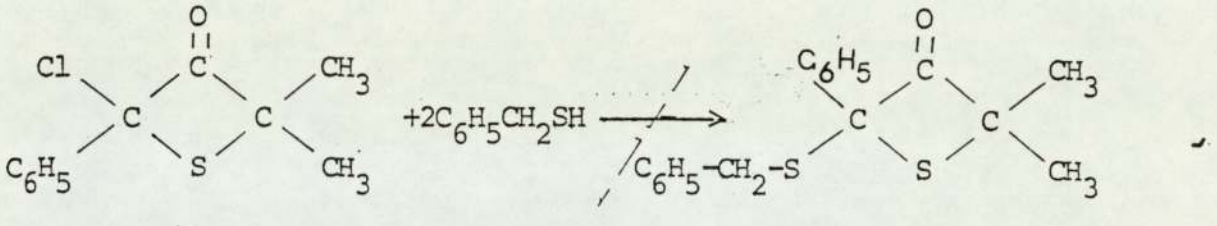
However, the mass spectrum of the methoxythietanone 99 did not show a parent ion at 222 mass units but gave the peaks at 190 and 194 in high abundance. An accurate mass spectrum on peaks 190 and 194 gave the molecular formula $C_{11}H_{14}O_2$ and $C_{11}H_{14}OS$ respectively. These molecular formula correspond to A and B.



The presence of peaks at 190 and 194 m/e suggest the compound is the methoxythietanone 99.

6 - a - 4: The benzylthiothietanone .

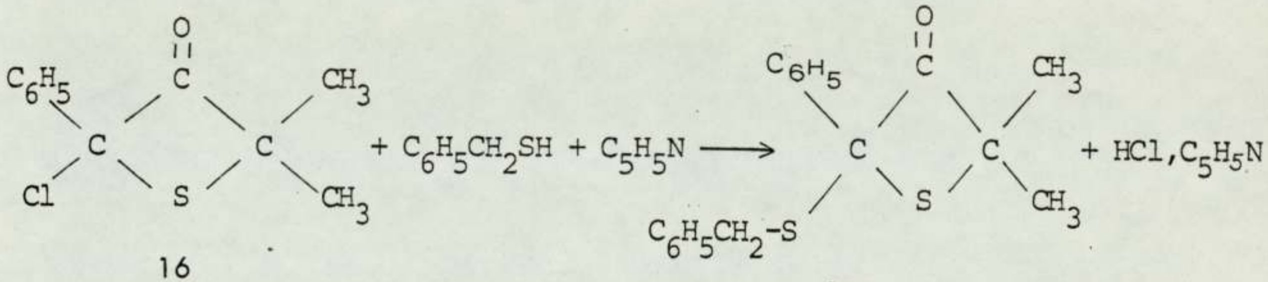
Although benzylmercaptan is a stronger nucleophile than methanol and hence the reaction of 2-chlorothietanone with benzylmercaptan is expected to be faster than with methanol, the treatment of one equivalent of 2-chlorothietanone 16 with two equivalents of benzylmercaptan did not yield the thietanone 100. This anomalous behaviour will be discussed in section (6-a-9).



16

100

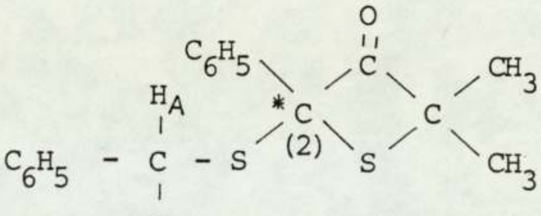
When the reaction of the chlorothietanone 16 with benzylmercaptan was carried out in the presence of one equivalent of pyridine, the product was the benzylthiothietanone 100.



16

100

The position of the carbonyl group at 1760cm^{-1} in the infrared spectrum confirmed the presence of a four-membered ring. The nuclear magnetic resonance spectrum of the product showed two singlets at δ = 1.5 and 1.75ppm; two doublets at δ =(3.7 -3.4) and (4.1 - 3.8)ppm and a multiplet at δ = 7.2ppm. Peaks at δ = 1.5, 1.75 and 7.2ppm were due to two methyl and phenyl protons. The methylene protons of the thietanone 100 were seen as two doublets. The two methylene protons have different chemical shifts, because carbon-2 is asymmetric and are therefore seen in the spectrum as an AB system. The AB spectrum always consists of four lines, two for the A part and two for the B part. The separation between the two lines in each pair is exactly equal. The relative intensity of methyl, methylene and phenyl protons is 6:2:10.

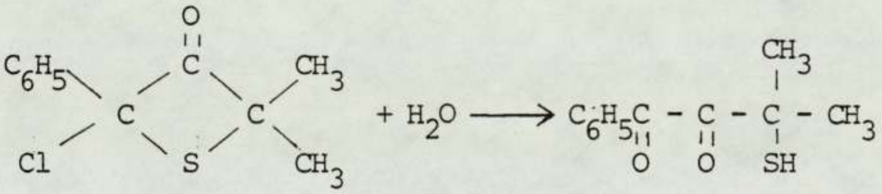


100

The elemental analysis agreed with molecular formula $C_{18}H_{18}OS_2$ for thietanone 100.

6 - a - 5: 3-Mercapto-3-methyl-1-phenyl-1,2-butanedione .

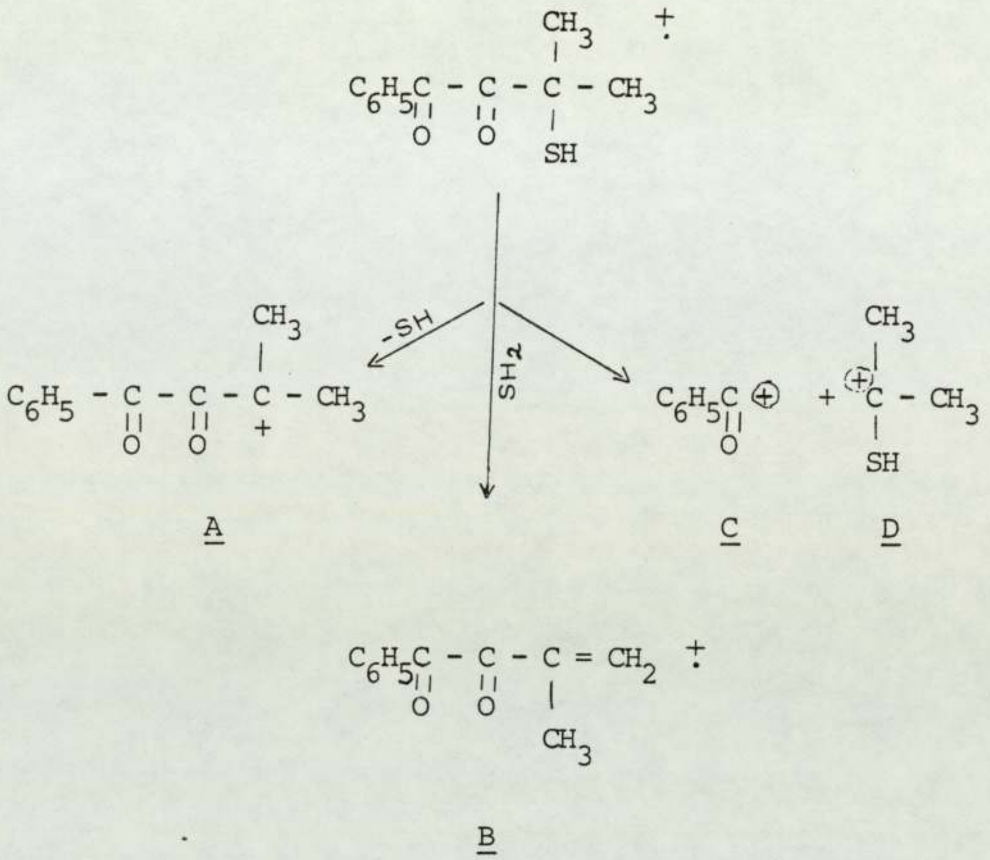
The treatment of the chlorothietanone 16 with water gave the diketone 101.



16

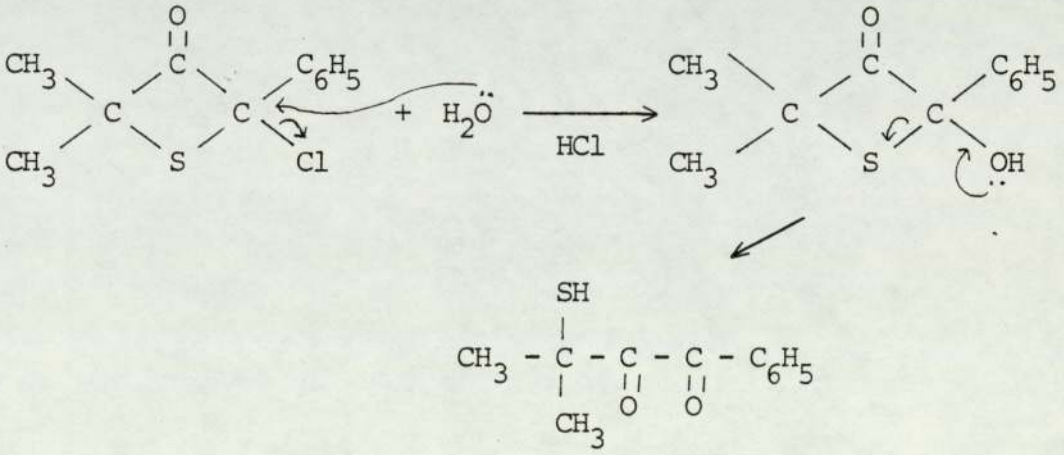
101

The spectroscopy data confirmed the formation of diketone 101.
The appearance of a weak peak at 2565 cm^{-1} in the infrared spectrum showed the presence of a thiol group. Strong bands at 1675 and 1715 cm^{-1} are due to the carbonyl groups. The carbonyl absorption of the diketone 101 is shifted about 70cm^{-1} to a lower wave number compared to the thietanone 16. The nuclear magnetic resonance spectrum of the diketone 101 showed peaks at δ=1.6, 2.1 and 7.1ppm due to methyl, thiol and phenyl protons respectively. The two methyl groups of the diketone 101 are equivalent so they are seen as a singlet in the spectrum. The molecular formula $C_{11}H_{12}O_2S$ was obtained by elemental analysis. The mass spectrum of the diketone 101 gave ion at $^m/_e$ 208 in low abundance. The major fragments are A, B, C and D.



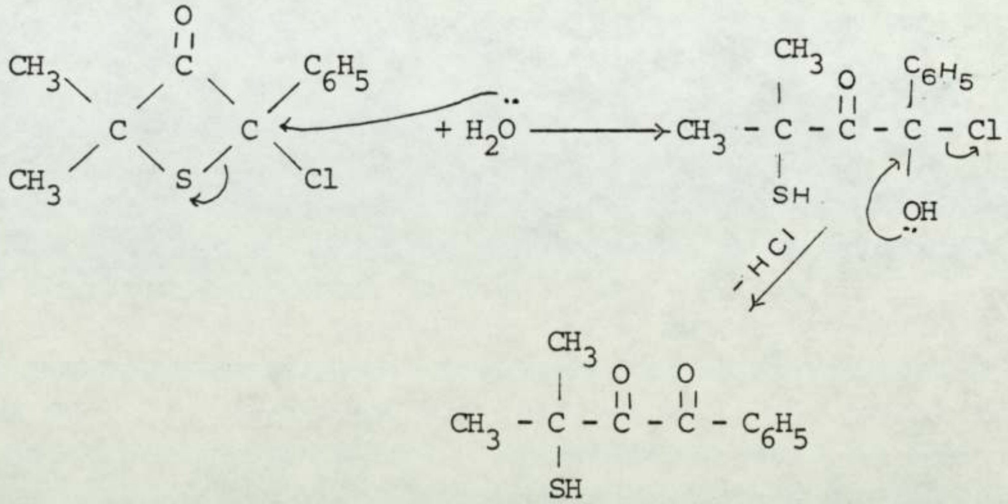
There are two possibilities for the mechanism of the reaction ··

(I) Replacement of chlorine by a hydroxyl group followed by ring opening.



101

(II) Ring-opening before elimination of the chlorine atom.

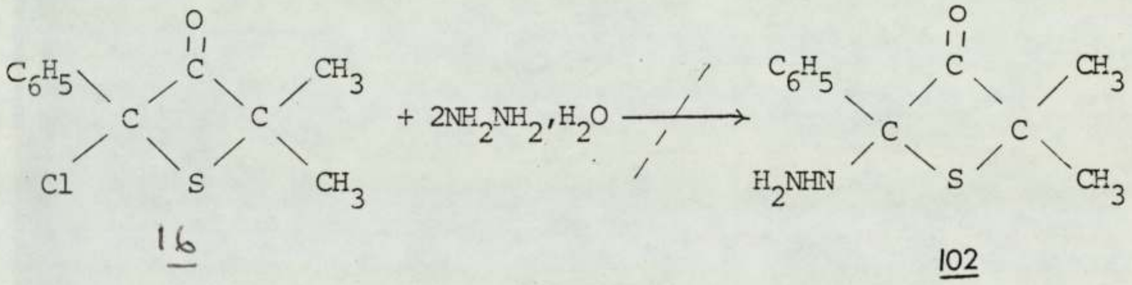


101

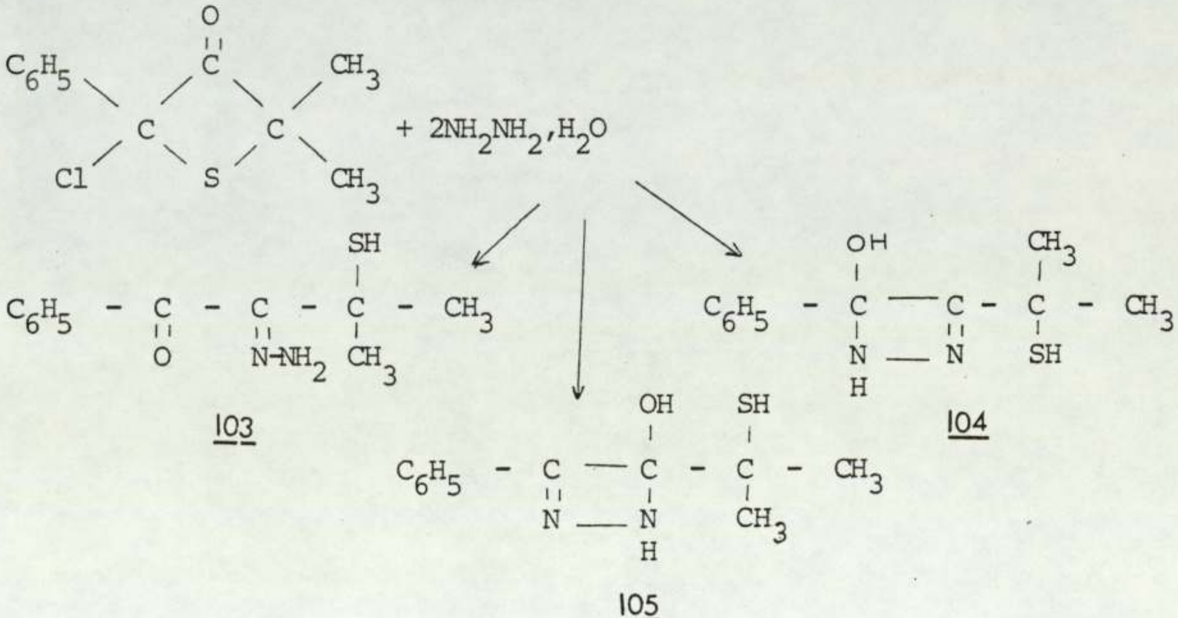
6 - a - 6: The reaction of thietanone* with hydrazine hydrate.

One equivalent of thietanone 16 was treated with two equivalents of hydrazine hydrate. The possible structure of the product was studied by spectroscopic methods. If hydrazine hydrate reacts in a similar manner to piperidine, morpholine and pyrrolidine, the product should be the thietanone 102. However, the absence of carbonyl group at 1760 to 1780cm^{-1} in the infrared spectrum and an absorption band at 2575cm^{-1} (thiol, S-H stretch) suggested that ring opening of 16 had occurred.

Hence:

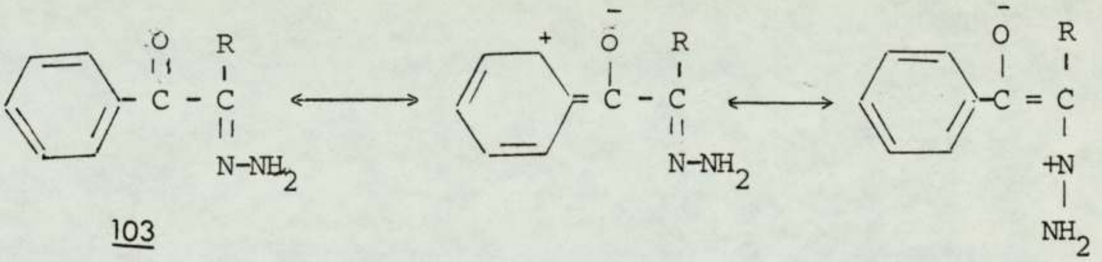


but

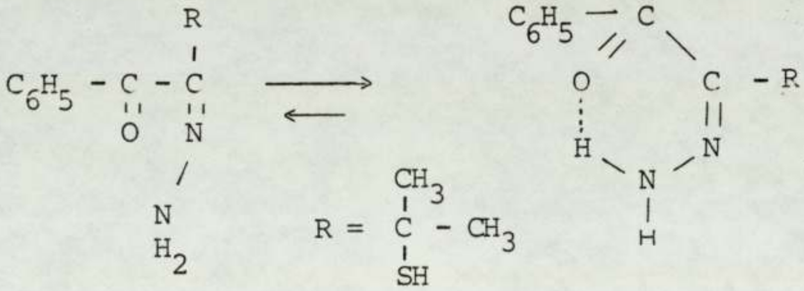


Ring opening could give rise to a variety of products as suggested above, e.g. 103, 104, 105

The infrared spectrum of the reaction product gave peaks at 3420, 3285, 2575, 1645, 1600, 1590 and 1550cm^{-1}. A peak at 1645cm^{-1} could be due to the carbonyl or carbon-nitrogen double bond (C=N) group. The position of the carbonyl group normally appears at approximately 1725cm^{-1}, however, conjugation and hydrogen bonding shift this band to lower wave number. Thus the absorption at 1645cm^{-1} could be attributed to the carbonyl stretch in 103.

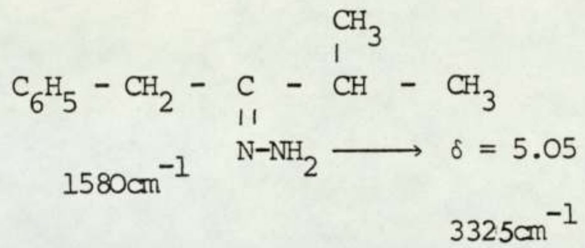


103



If the carbonyl absorption of the compound 103 was at 1645cm^{-1} where would the C=N stretching absorption be? The C:N stretch in amines, oximes, etc., gives a variable intensity absorption in the range from 1690 to 1540cm^{-1}.

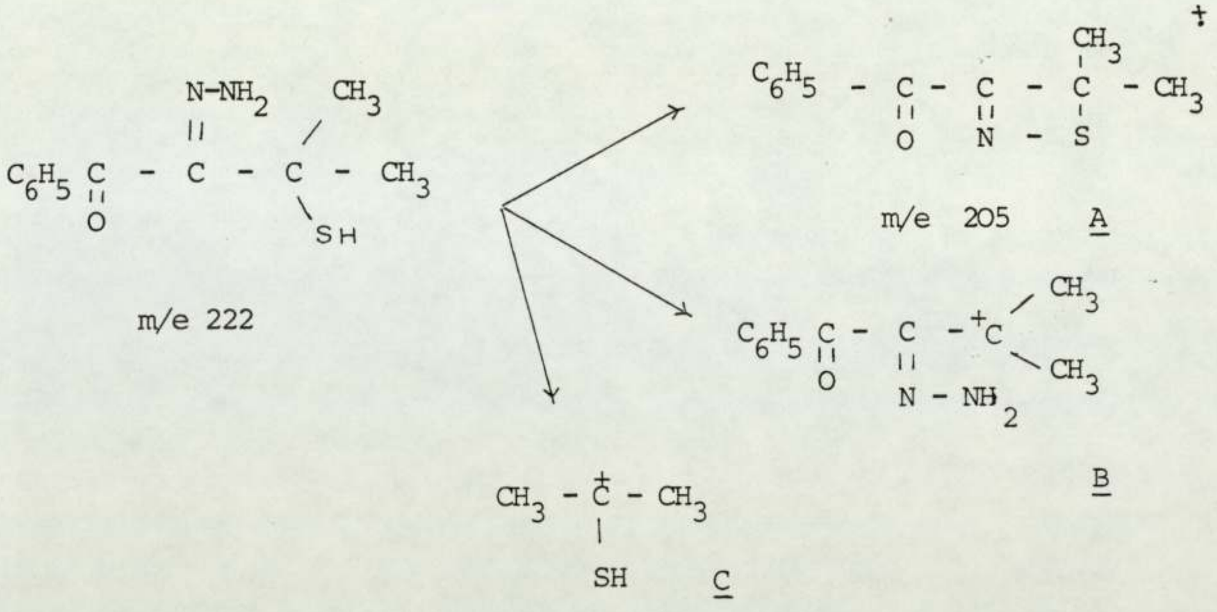
The carbon-nitrogen double bond (C=N) stretch in the hydrazono-compound 106 has been found to be at 1580cm^{-1}.



$$C_6H_5-CH_2-\underset{\underset{\displaystyle N-NH_2 \longrightarrow \delta = 5.05}{\|}}{C}-\overset{\overset{CH_3}{|}}{CH}-CH_3$$

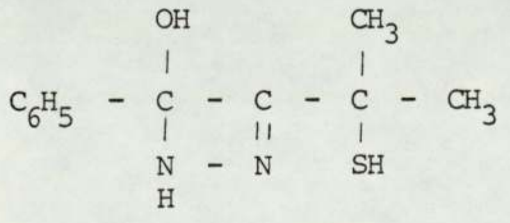
<u>106</u>

However, the infrared spectrum of the product showed medium peaks at 1590cm^{-1} and 1600cm^{-1}, but these peaks might not belong to the C=N stretch because it is not possible to say definitely what these frequencies correspond to. The position of peaks at 3420cm^{-1} and 3285 cm^{-1} correspond to the imino (N-H) or hydroxyl (O-H) stretching frequencies. The infrared spectrum of the product showed the presence of two bands at 3285 and 3420cm^{-1}. These bands suggest the presence of hydroxyl (O-H) stretch (3420 cm^{-1}) and imino (N-H) stretch (3285cm^{-1}). This is evidence for <u>104</u> and <u>105</u>. Thus the infrared spectrum data is inconclusive. The nuclear magnetic resonance of the product gave peaks at δ = 1.75, 3.05, 6.15 and 7.35ppm in relative intensity 6:1:2:5 which could agree with structures of compounds <u>103</u>, <u>104</u> or <u>105</u> A peak at δ = 6.15ppm in the spectrum of the product might be due to amine protons. For further evidence the nuclear magnetic resonance spectrum of the hydrazono-compound <u>106</u> showed amino protons at δ = 5.05ppm. Thus the peak at δ = 6.15 ppm does not appear to correspond to the amino (NH_2) group of <u>103</u>. The mass spectrum of the product gave ions at m/e 222, 205, 190, 119, 103, 104 and 75. If the compound <u>103</u> is the product of the reaction it would be possible to draw fragments <u>A</u>, <u>B</u> and <u>C</u> for the ions at $\frac{m}{e}$ 205, 190 and 75. However, the ions at $\frac{m}{e}$ 119, 103, 104 would not fit into this fragmentation pattern. Furthermore for structure <u>103</u> the ion at $^{m}/_{e}$ 105 ($C_6H_5\underset{\underset{O}{\|}}{C}+$) would be expected to occur in high abundance.

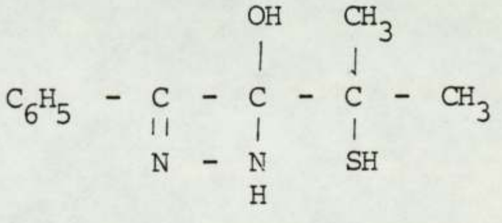


The ^{13}C nuclear magnetic resonance spectrum did not reveal the presence of a carbonyl group between 170 - 210ppm. Thus the spectroscopic data does not fully agree with structure 103 and suggests that the product must be 104 or 105.

Interpretation of the infrared spectrum of the product in terms of it being 104 or 105 .

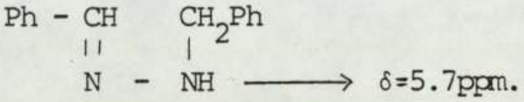


104



105

The peak at $1645cm^{-1}$ is due to carbon-nitrogen double bond (C=N) stretch The imino (N-H) and hydroxyl stretch are seen at 3420 and $3285cm^{-1}$ and a weak peak at $2575cm^{-1}$ is due to the thiol (S-H) group in the infrared spectrum. Peaks at 1590 and $1600cm^{-1}$ are due to imino (N-H) deformation. The peak at $\delta = 6.15$ppm in the nuclear magnetic resonance spectrum is likely to be due to an overlap of imino (N-H) and hydroxyl (O-H) resonances (due to proton exchange). For more information the nuclear magnetic resonance of 107 was studied.(121) The chemical shift of the imino (N-H) proton in structure 107 is at δ = 5.7ppm.

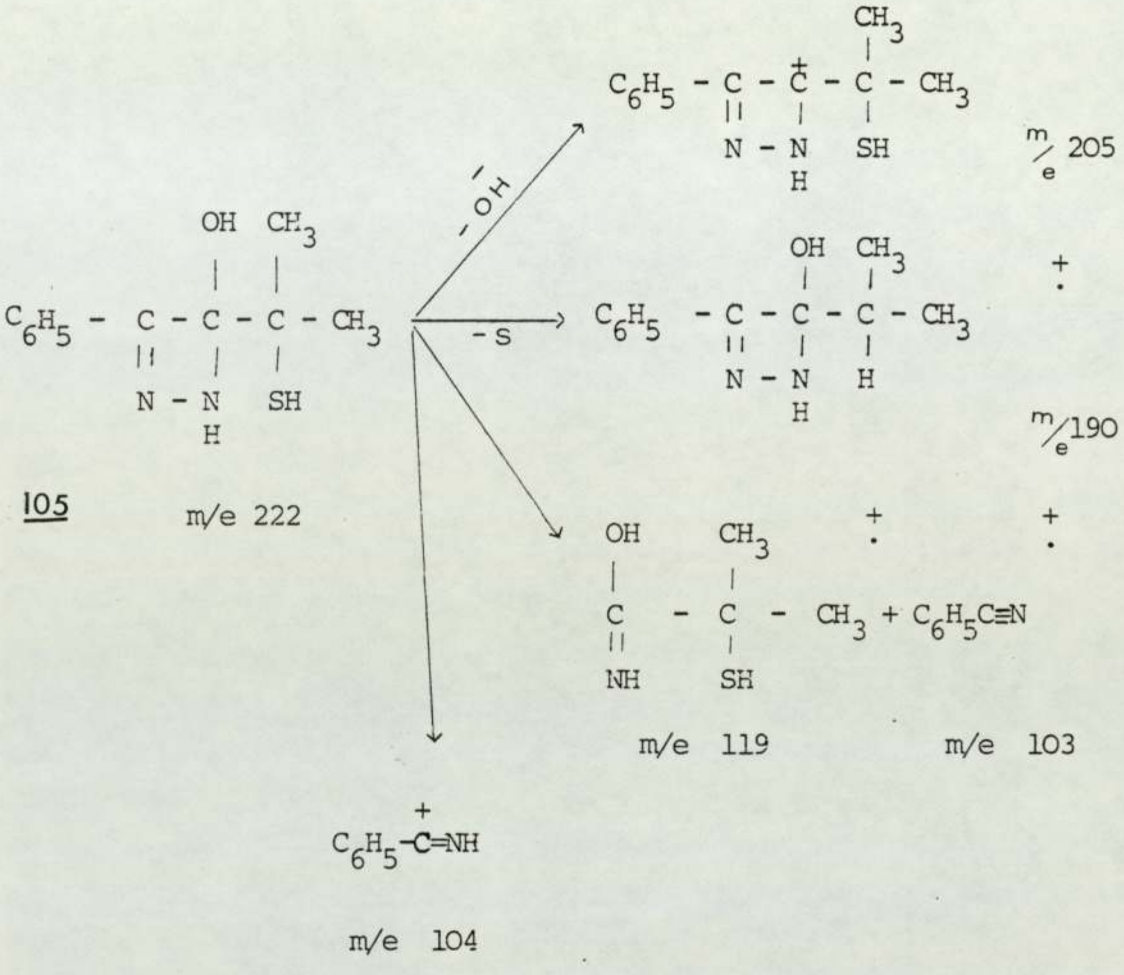


$$\begin{array}{ll} \mathrm{Ph - CH} & \mathrm{CH_2Ph} \\ \quad\;\, \parallel & \;\; | \\ \quad\;\, \mathrm{N} \; - & \mathrm{NH} \longrightarrow \delta = 5.7\mathrm{ppm.} \end{array}$$

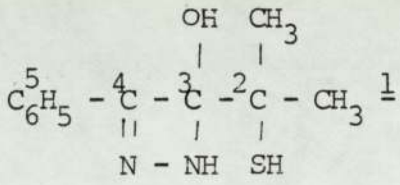
107

Thus the peak at δ = 6.15ppm in the spectrum of the product could be due to imino (N-H) and hydroxyl protons. There is not a lot of difference between the infrared spectra of the two structures 104 and 105.

If the product was compound 104, the phenyl protons in the nuclear magnetic resonance would occur as a singlet. If the product was compound 105, the phenyl protons would occur as a multiplet. The recorded spectrum showed a multiplet peak for phenyl protons, suggesting that the product is in fact 105. The presence of ions at $\frac{m}{e}$119, 103, 104 can also easily be explained in terms of structure 105.



^{13}C chemical shifts (ppm) in structure 105

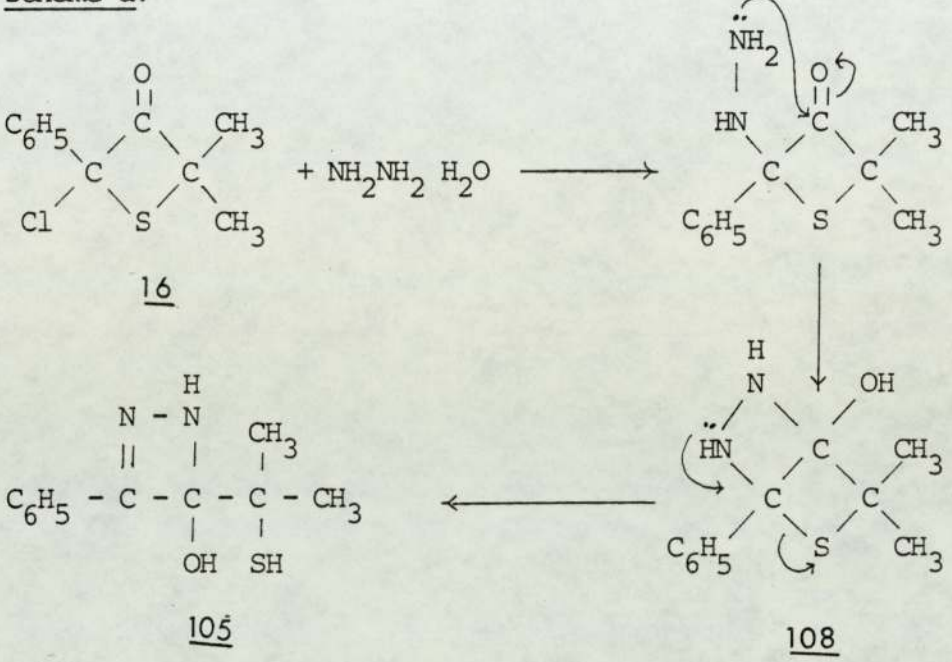


Chemical shifts	carbon 1	carbon 2	carbon 3	carbon 4	carbon 5
	30	48	96	128·734	129·059

The mechanism of the reaction is probably via scheme a.

The first stage is nucleophilic attack on carbon-2 to give 108, followed by C-S cleavage bond.

Scheme a:

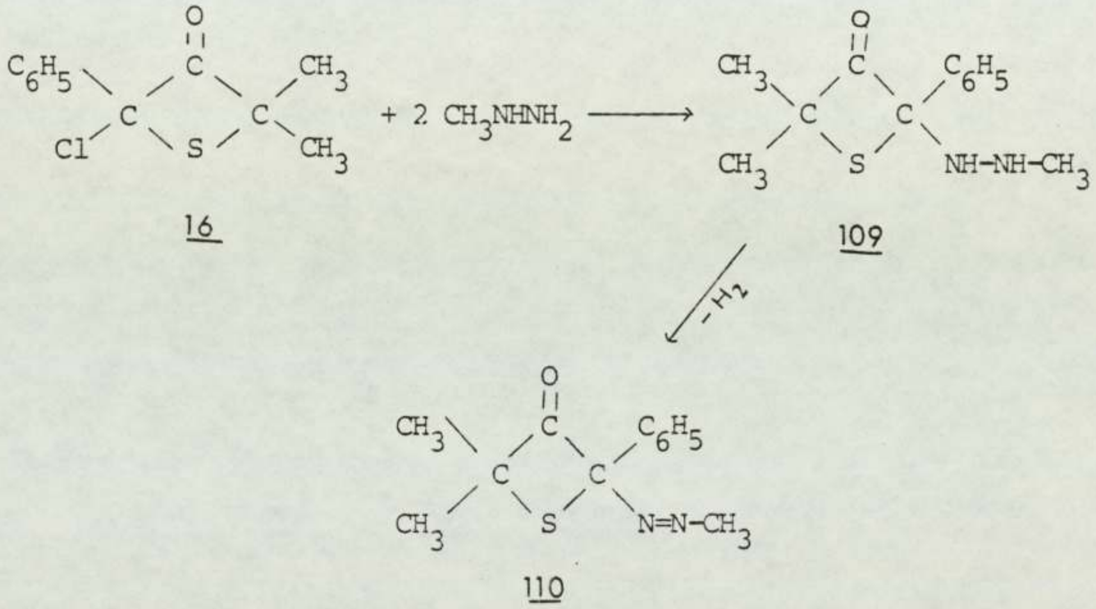


6 - a - 7: The reaction of thietanone* with Methylhydrazine .

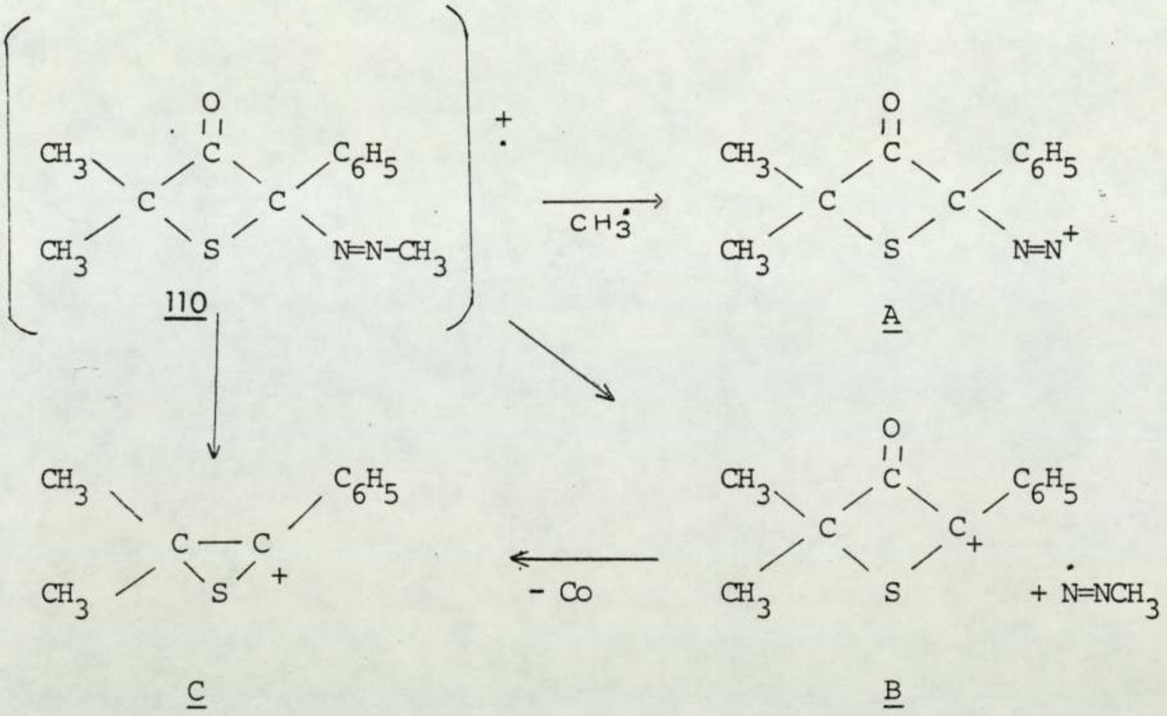
Treatment of 2-chloro-4,4-dimethyl-2-phenylthietan-3-one with methylhydrazine gave a mixture of three compounds. The fraction which is insoluble in ether was methylhydrazine hydrochloride. The melting point, infrared spectrum and solubility in water of the white solid agreed with those of methylhydrazine hydrochloride.
Column chromatography was used for the purification of the liquid fraction and two fractions were collected.

Analysis of fraction (I)

The infrared spectrum showed a peak at $1765 cm^{-1}$ due to a carbonyl group on a four-membered ring. The nuclear magnetic resonance spectrum showed peaks at $\delta = 1.6, 1.5, 1.2$ and 7.3ppm and are due to three methyl and a phenyl group respectively. The mass spectrum show a parent ion peak at 234 mass units. The presence of a carbonyl band at 1765cm^{-1} and the absence of carbon-chlorine and nitrogen-hydrogen bands in the infrared spectrum and the formation of methylhydrazine hydrochloride suggest the product might be the thietanone 110.

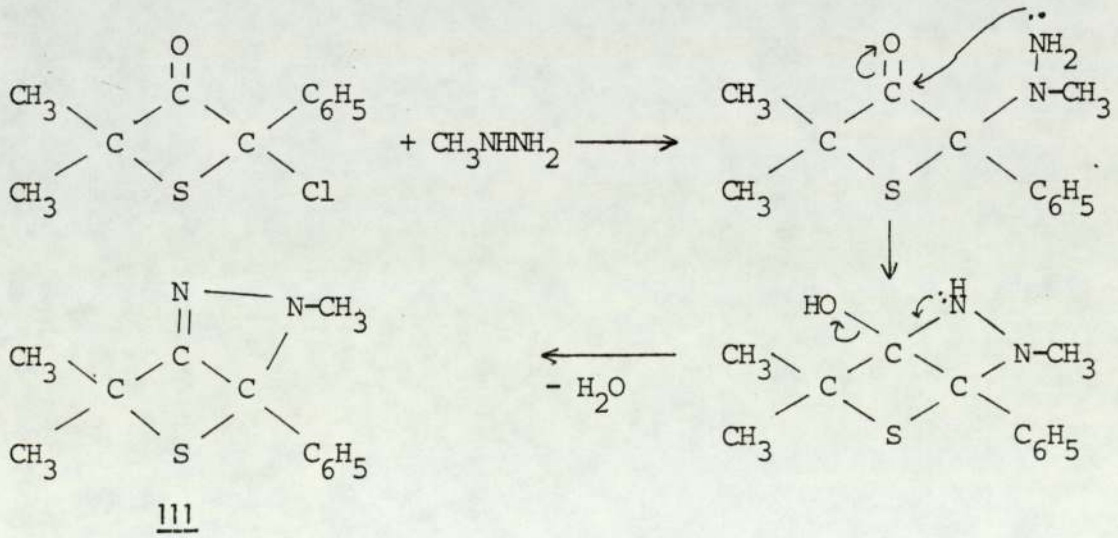


It is suggested that the thietanone 16 on treatment with methylhydrazine gives 109 in the first stage and the dehydrogenation of the 109 gives 110. However, the dehydrogenation of the 109 is unusual, but the absence of imino proton (N-H) in the nuclear magnetic resonance spectrum suggest the structure 110 The mass spectrum of the Fraction 1 gave ions at $\frac{m}{e}$ 238,234, 224, 219, 163 . The ions at $\frac{m}{e}$ 238, 234 have a low abundance (about 15%) and peaks at 224, 219 and 163 have high abundance. The analysis of the ions at $\frac{m}{e}$ 238 and 224 was not possible for the suggested structure 110. The ions at $\frac{m}{e}$ 219, 191,163 could be due to fragments A, B and C.



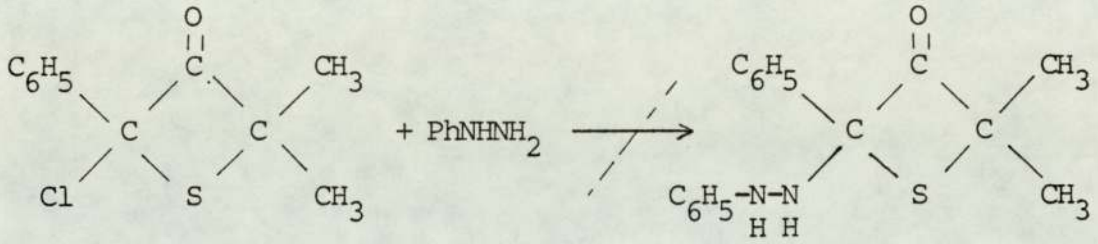
Analysis of Fraction 2

The presence of the carbon-nitrogen double bond (C=N), absence of the carbonyl group and formation of water in fraction 2, suggest structure 111 for fraction 2. Methylhydrazine has two nucleophilic centres (NH and NH_2). Attack of the amine (NH_2) group on carbon-2 gave thietanone 110 and attack of the imino group on carbon-2 gave 111.



6 - a - 8: The reaction of thietanone* with phenylhydrazine .

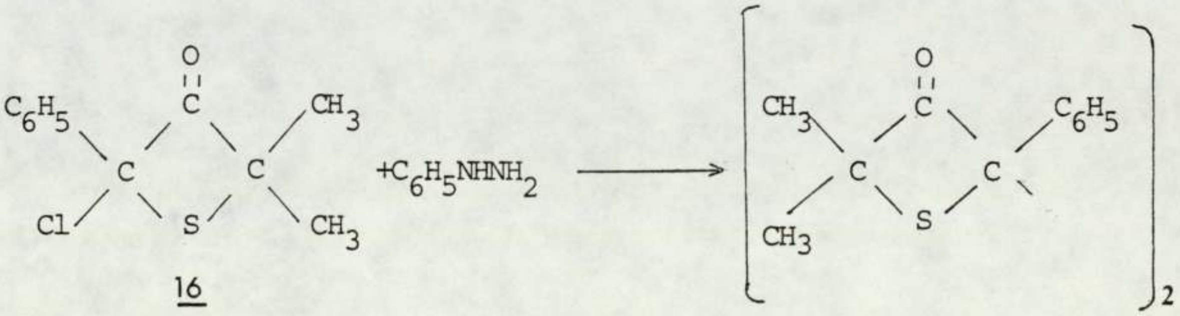
One equivalent of the thietanone 16 was treated with two equivalents of phenylhydrazine. The product was expected to be the thietanone 112. However, the position of the carbonyl group in the infrared spectrum agreed with the structure 112 but the mass spectrum and nuclear magnetic resonance spectrum contraindicate structure 112.



16

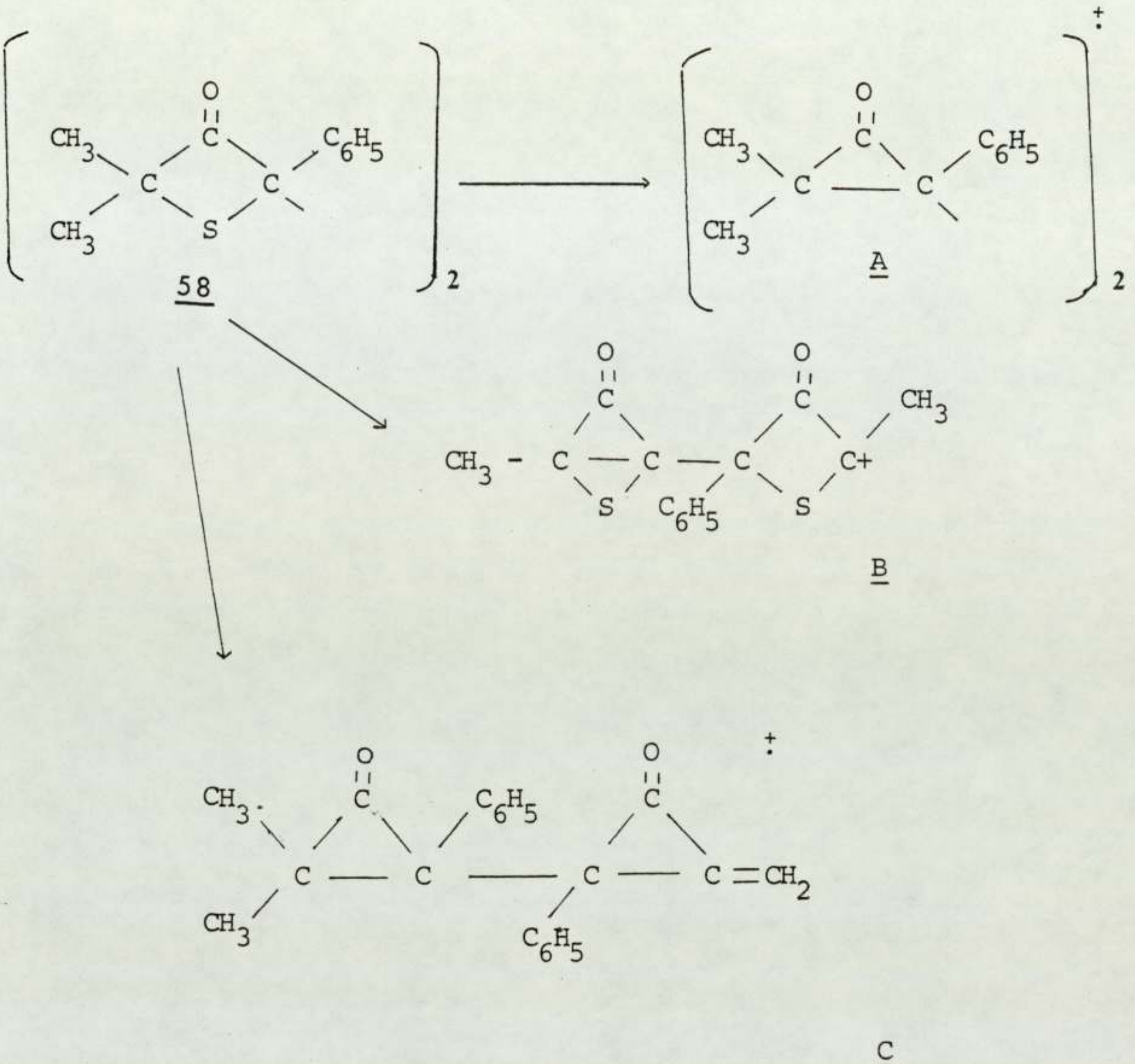
112

The nuclear magnetic resonance spectrum of the product showed two singlets and one multiplet due to methyl and phenyl protons in relative intensity 6:5. The mass spectrum gave a parent ion at 382 mass units. The ions at $\frac{m}{e}$318, 302, 275 are attributed to the fragments A, B and C. These findings agreed with structure 58. The elemental analysis confirmed the structure of 58.



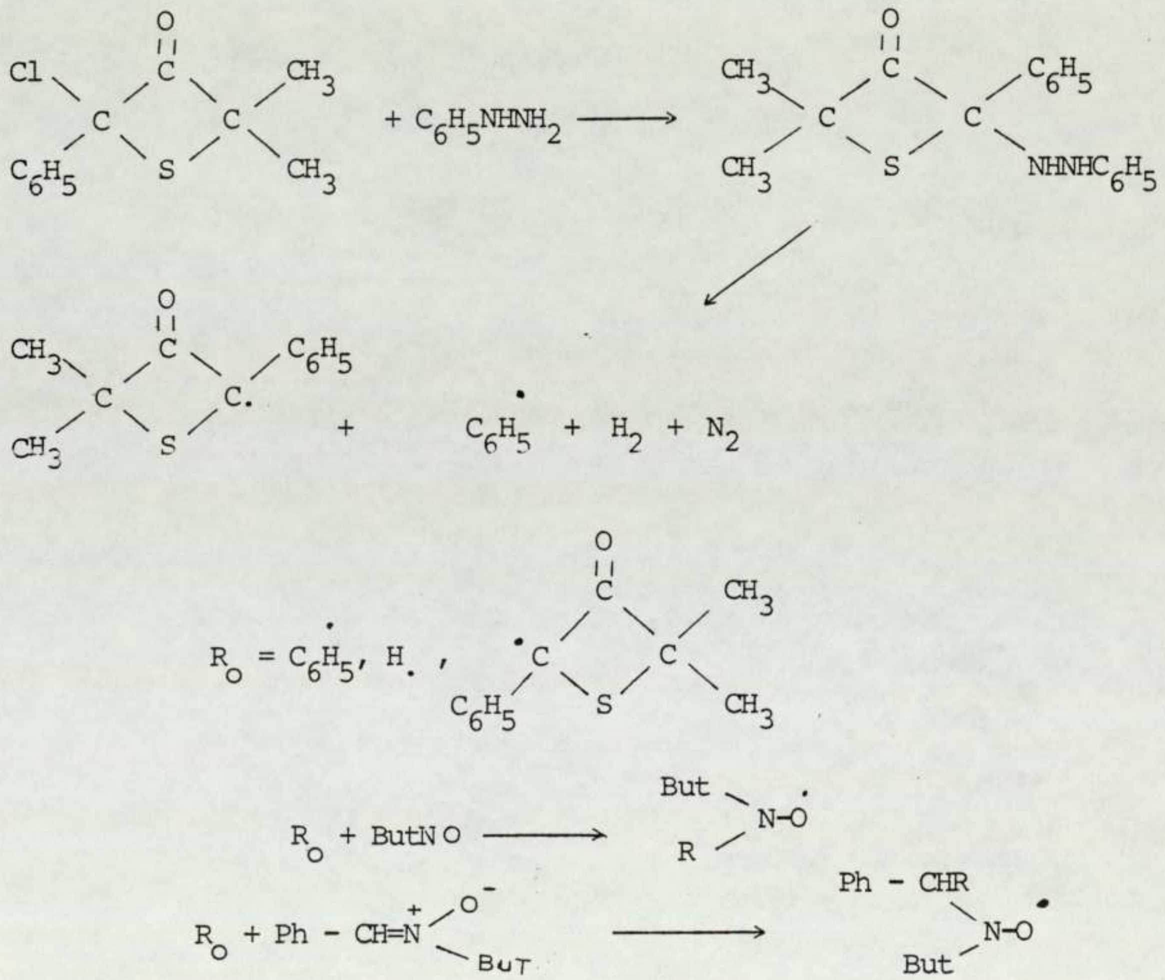
16

58


58
A
B
C

The reaction might proceed via a radical. The electron spin resonance spectrum of the reaction mixture was carried out in the presence of a spin trap <u>113</u> .

A suitable radical scavenger which can react with any radical intermediate to form a relatively long-lived radical scavenger is frequently referred to as a spin trap, e.g.
nitroso-compounds or nitrones, both of these react rapidly with a variety of short-lived radicals.



<u>113</u>

However, the electron spin resonance spectrum showed the existence of a radical in the reaction mixture but there is no firm evidence that the reaction proceeds via a radical because phenylhydrazine (starting material) in the presence of a spin trap also gave a radical. We contend that phenylhydrazine is able to react with the oxygen of the air via a radical and this radical in the presence of spin trap 113 could be detected by e.s.r. So the mechanism of the reaction could be studied by the methods outlined below.

1) detect the radical in the mixture of the reaction by using e.s.r. methods at low temperature.
2) determine the existence of a radical in the reaction mixture, in the presence of a spin trap and in the absence of air.

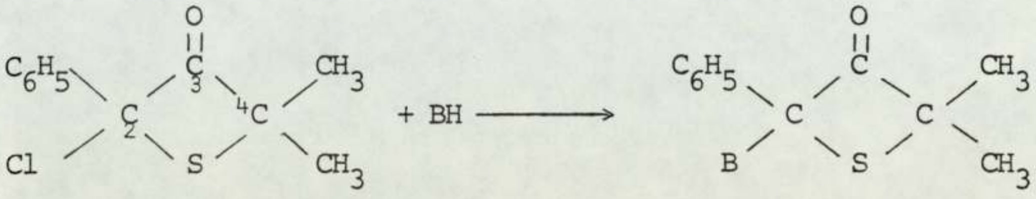
6 - a - 9: The reactivity of carbon-2 and carbon-3 of 2-chloro-4,4-dimethyl-2-phenylthietan-3-one.

It was prudent to study the reactivity of C-2 and C-3 of the thietanone 16 towards nucleophiles and relate the reactivity to the hard and soft acid and base (H.S.A.B.) rules. The (H.S.A.B) theories have been reviewed by a number of authors.$^{(122-124)}$

According to this theory, the reactivity of nucleophiles increases in the order $\bar{O}H > O\bar{C}H_3 > R\bar{N}H > R\bar{S}$,
and the"hardness" sequence of carbanions follows the order $sp > sp^2 > sp^3$.
Higher P character increases softness.

The 2-chlorothietanone 16 has two electrophilic centres with differing hardness (C-2 and C-3), therefore nucleophiles could attack at either of these two centres, depending on their degree of hardness or softness.

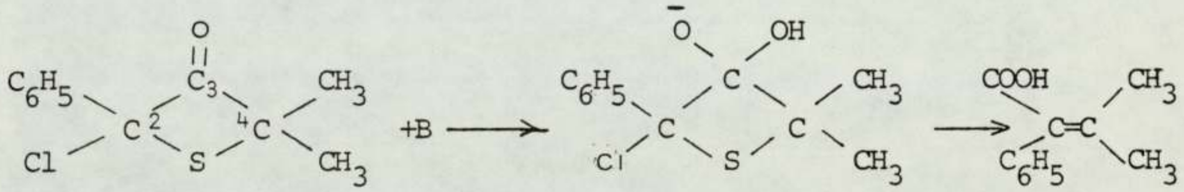
1: nucleophilic attack on C-2



16

$B = \diagdown\underset{H}{N}\diagup$, CH_3OH , $C_6H_5CH_2SH$, H_2O

2: attack on the C-3

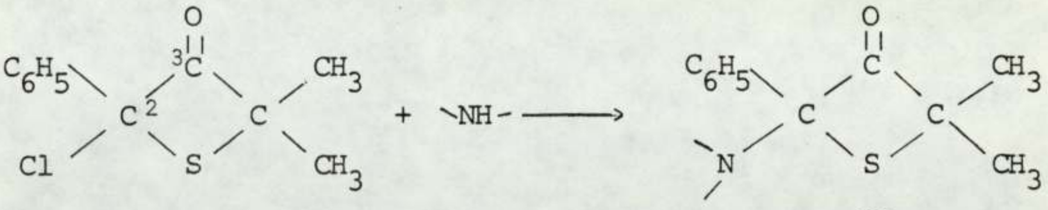


16

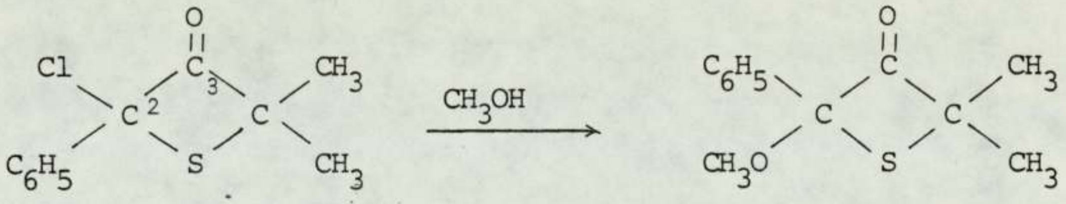
$B = \overline{OH}$

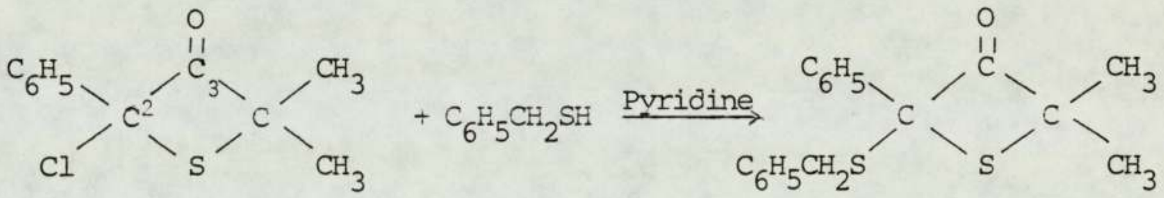
The carbonyl group has a hard acceptor carbon for electrophilic attack, hence hard bases prefer to attack the carbonyl carbon. Soft bases normally do not attack a carbonyl carbon under mild conditions. Thus nucleophiles such as hydroxyl ($O\bar{H}$) will readily attack the carbonyl carbon, but nucleophiles such as methanol (CH_3OH) amine (RNH_2) alkyl mercaptan (RSH) will not. C-2 being softer than the carbonyl however, will be readily attacked by these latter nucleophiles. From classical theory that a strong acid and strong base form a stable bond, a weak acid and base will form a less stable one so hard acids (acceptors) tend to form strong bonds with hard bases (donors).

The reaction of 2-chlorothietanone 16 with nucleophiles gave the thietanones 98, 99 and 100.



-NH- = piperidine, morpholine, dimethylthietanone, pyrrolidine

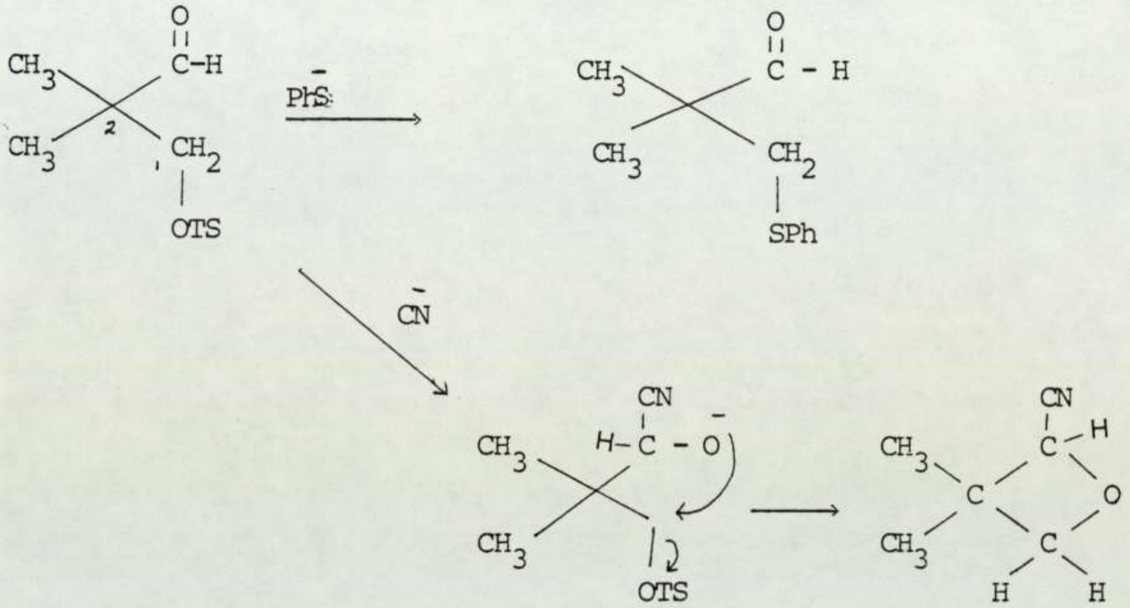




These bases are not hard enough to attack the carbonyl group under mild condition. The chemical reactivity of the above nucleophiles with C-2 is more favoured than with the carbonyl group because -

1 : The entering and leaving groups are bonded to tetrahedral carbon hence they have a similar hardness value. Nerdel et al.(125) have also found that when 3-tosyloxypivaldehyde is treated with a hard and a soft base ($C\bar{N}$, $Ph\bar{S}$), the $Ph\bar{S}$ attacks exclusively at C-1 and the CN^- attacks exclusively at the carbonyl group.

This suggests that $R\bar{S}$, $CH_3\bar{O}$, $R_2\bar{N}$, H_2O will not attack the carbonyl group of the thietanone 16.

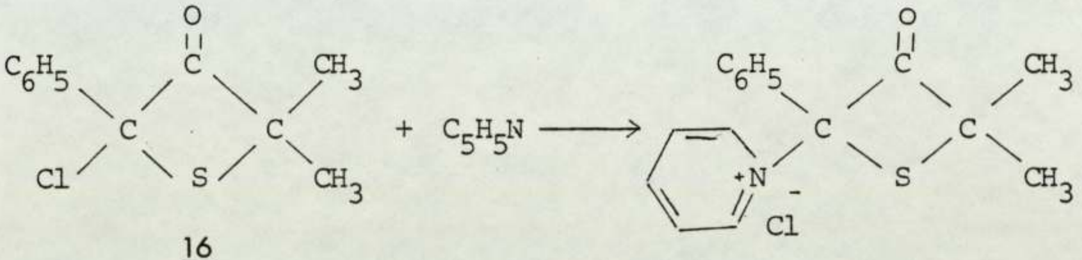


2 : Amines (R_2NH), methanol, (CH_3OH), water (H_2O) are harder bases than chlorine ($C\bar{l}$) and softer than hydroxyl ($\bar{O}H$) hence these bases will only attack on the C-2 releasing the $C\bar{l}$ as a leaving group. If we consider the reaction

$$A' + AB \longrightarrow A'B + A$$

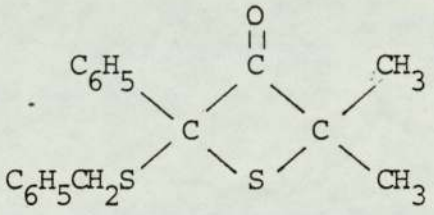
A' will react with AB only provided A' is a stronger Lewis acid than A.

In general the softness of an acceptor or base increases on going down a column in the periodic table, and hardness increases on going across the periodic table. If chlorine ($\bar{Cl}$) is compared with $R\bar{S}$, then both of them are in the same row in the periodic table but the electronegativity of the chlorine atom is greater than sulfur, so benzylmercaptan is softer than chlorine ($\bar{Cl}$). Although the treatment of the chlorothietanone 16 with benzylmercaptan did not give the benzylthiothietanone 100, compound 100 was formed when the chlorothietanone 16 was treated with benzylmercaptan in the presence of pyridine. This may be because the pyridine being harder base than benzylmercaptan attacks the carbon-2 of the chlorothietanone 16 to form the pyridinium chloride 114. The pyridinium chloride 114 in the presence of benzylmercaptan gives the benzylthiothietanone 100. The softness of the ($\bar{Cl}$) is increased by the formation of the pyridinium chloride intermediate.



16

114



100

The order of hardness is

$$\bar{O}H > \bar{C}l \qquad \bar{C}l > R\bar{S} \qquad R\bar{S} > C_5H_5\overset{+}{N}\,\bar{C}l$$

It is for this reason that the reaction of benzylmercaptan with thietanone does not proceed significantly at room temperature whereas chlorothietanone 16 reacts rapidly with piperidine, morpholine, pyrrolidine and methanol under the same conditions. In terms of nucleophilicity one would have expected the benzylmercaptan to react with chlorothietanone 16 faster than the reaction of methanol with thietanone. However, this was not so. This may be rationalized using the hard and soft base theory as described already and this suggests that due to ring strain, the C-2 may have more sp^2 character than sp^3, hence retarding the effect for R$\bar{S}$.

In general, rates of nucleophilic reaction on the sp and sp^2 carbon atoms such as nitrile and carbonyl are mainly controlled by basicity rather than polarizability of the nucleophile used (126, 127) while in the case of the sp^3 carbon atom polarizability is a more important factor than basicity. According to the above ideas it appears that the properties of the C-2 of the chlorothietanone <u>16</u> are closer to an sp^2 than to an sp^3 carbon. Potapov(102) has stated that for small three- and four-membered rings, the strain energy is very high, and in order to accommodate this high ring strain, the bond angles significantly deviate from the normal tetrahedral value. The chemical properties of the chlorothietanone <u>16</u> confirm this deviation from sp^3 $\longrightarrow$ sp^2.

6 - a - 10: <u>α - Effect</u> .

It was found that hydrazine hydrate is able to attack the hard acceptor (carbonyl group). However, hydrazine and methylhydrazine are not harder than piperidine and morpholine (see Table 22), but they are able to attack the carbonyl carbon. This anomalous behaviour may be explained by the α -effect. Ibne-Rasa and Edwards(128) have ascribed the greater reactivity of such nucleophiles to stabilization of the activated complex by the lone pair of electrons on the α- atom and have designated the rate-enhancing effect as the α-effect.

Table (22) PK_a of several nucleophiles.

PK_a of the nucleophilic reaction of p-nitrophenyl acetate in water.(119, 120)

Nucleophile	PK_a	^oC
Hydrazine	8.1	25
Piperidine	11.2	30
Morpholine	8.7	30

Homoconjugation and acid dissociation constants of protonated monoamines in acetonitrile(AN) as solvent.

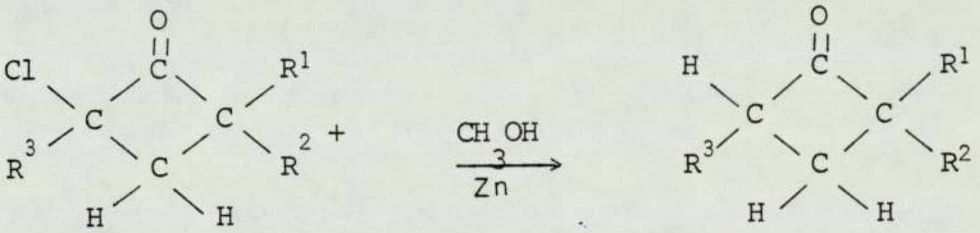
Amine	PK_a(W)	PK_a(AN)
Piperidine	11.22	18.92
Pyrrolidine	11.27	19.58
Morpholine	8.36	16.61

6 - b: The reduction of thietanone*.

The reduction of alkyl halides by various reducing reagents has been reviewed (129) and depends on the structure of the alkyl halides. One of the general reduction methods is that of Grignard reagents with active hydrogen compounds.

$$\mathrm{R{-}Cl + Mg \longrightarrow RMgCl + X\,H \longrightarrow RH + Mg\,ClX}$$

Some α-haloketones can be reduced by zinc in the presence of methanol e.g. the dibromoketones and the chlorocyclobutanone. (130, 131)



The reduction of the 2-chlorothietanone 16 was attempted by these methods.

(I) Using magnesium as a reducing reagent.

The chlorothietanone 16 was treated with magnesium at room temperature, then methanol was added to the mixture. Two liquid and solid fractions were collected.

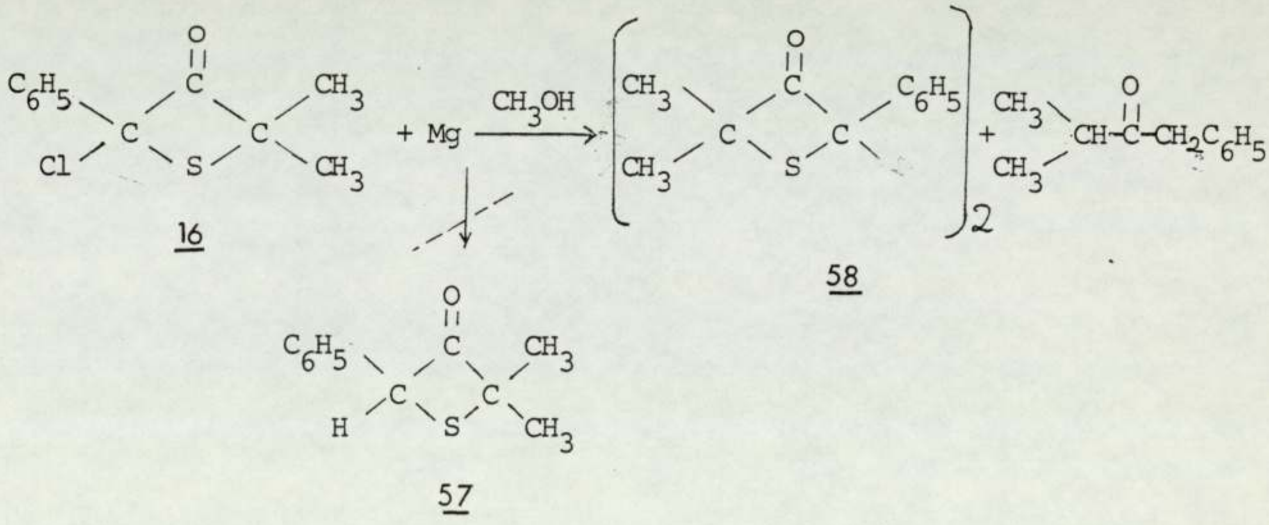
Analysis of liquid fraction

The infrared spectrum of the liquid fraction showed a peak at 1710 cm^{-1} due to carbonyl group. The nuclear magnetic resonance spectrum gave doublet, septet, singlet and singlet peaks at δ = 0.9, 1.6, 3.5, and 7. 2ppm respectively of relative intensity 6:2:1:5.

The mass spectrum gave a parent ion peak at 162 mass units. These findings agreed with the formation of benzyl isopropyl ketone.

Analysis of solid fraction

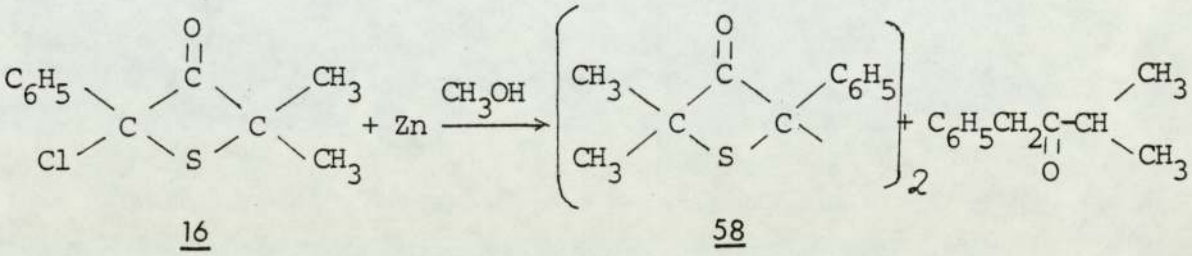
The infrared spectrum of the solid fraction showed peaks at 1760cm^{-1} due to a carbonyl group and the position of the carbonyl group absorption showed the presence of a four-membered ring. The nuclear magnetic resonance spectrum gave two singlet peaks due to methyl protons and the phenyl group was at $\delta = 7.1$ppm. However, the position of the carbonyl group in the infrared spectrum agreed with the formation of the thietanone 57 but the nuclear magnetic resonance spectrum disagreed with structure 57. According to structure 57 a methine proton should appear at about $\delta = 3.9$-4.2ppm in the nuclear magnetic resonance spectrum. However, the recorded spectrum did not contain a peak in this position. The mass spectrum gave a molecular ion peak at 382 mass units. The spectroscopy data confirmed the formation of 58.



Treatment of Chlorothietanone 16 with magnesium in THF (see Page 109) gave benzyl isopropyl ketone.

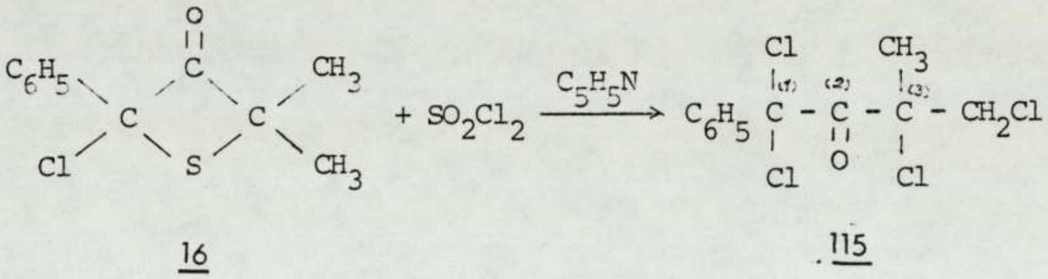
(II) Using zinc as reducing reagent.

Treatment of the thietanone 16 with zinc followed by the addition of methanol to the mixture gave the dithietanone 58 and benzyl isopropyl ketone as described in p.198.



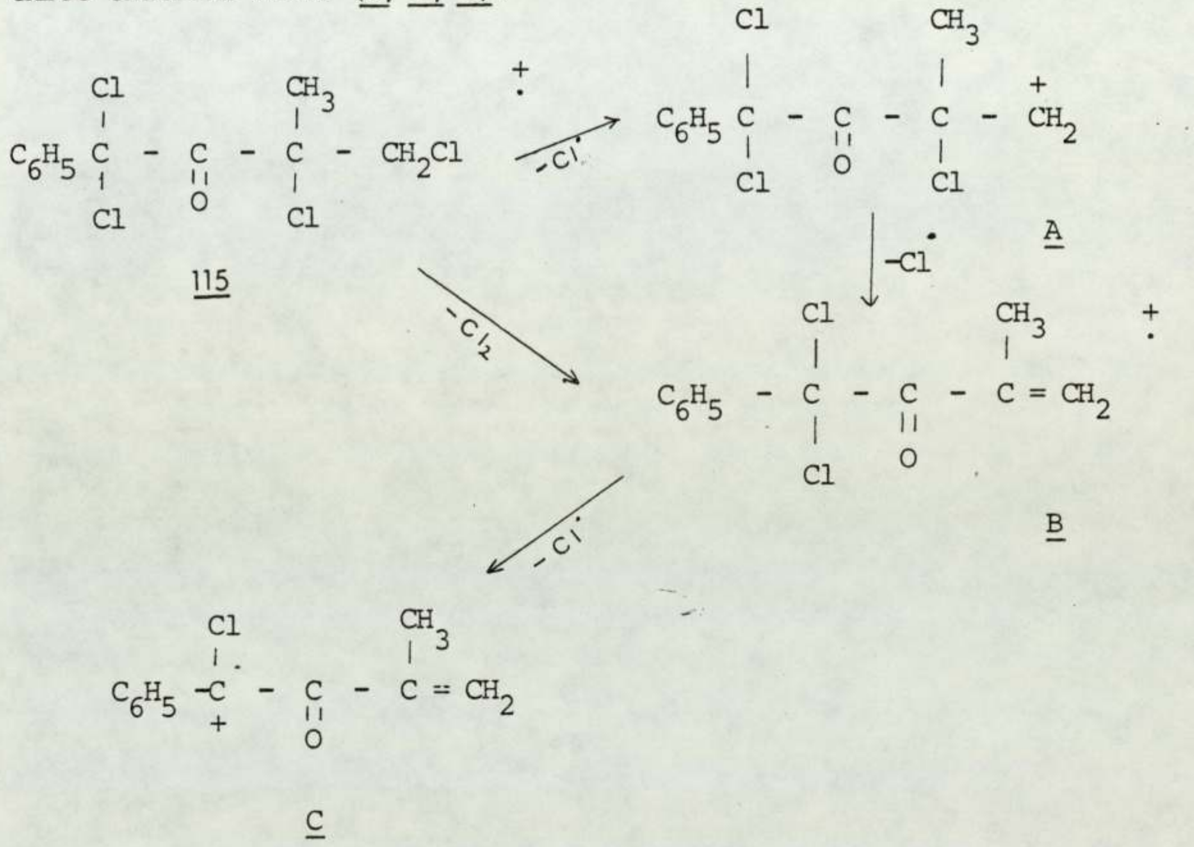
6 - c: Chlorination of thietanone* by sulfuryl chloride.

Treatment of the chlorothietanone with sulfuryl chloride in the presence of pyridine gave the butanone 115.



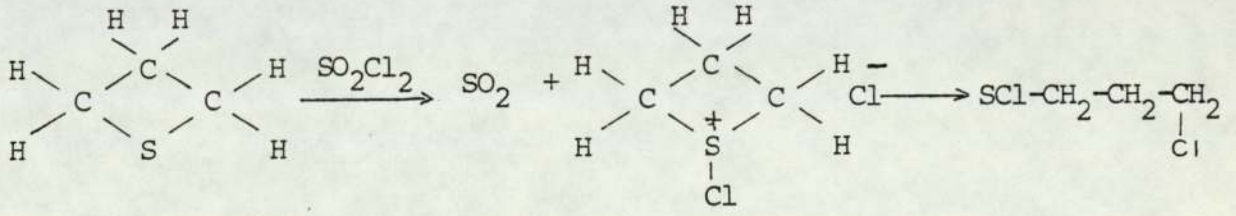
The infrared spectrum of the product showed a peak at 1730 cm^{-1} due to the carbonyl group of the butanone 115. The nuclear magnetic resonance spectrum gave peaks at $\delta = 1.9$, 3.75, and 7.6 ppm, due to methyl, methylene and phenyl groups respectively with relative intensities 3:2:5. Methylene protons appeared as an AB system because carbon-3 is asymmetric. The mass spectrum of the butanone 115 showed a parent ion peak at 298 mass units. The relative intensity peaks at M, M+2, M+4, M+6 and M+8 confirmed the presence of four chlorine atoms in the molecule.

The accurate mass spectrum of an ion at $\frac{m}{e}$ 298 gave the molecular formula as $C_{11}H_{10}Cl_4O$. The major fragments are due to loss of one, two and three chlorine atoms (A, B, C).



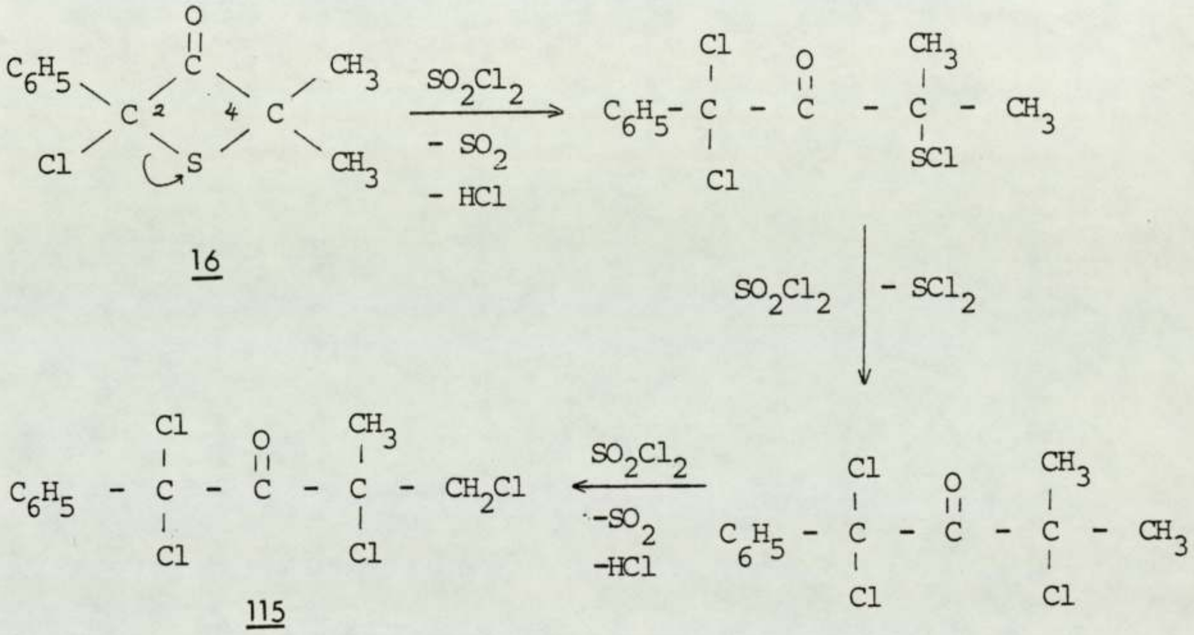
The reaction probably proceeds via carbon-sulfur cleavage similar to that encountered in the reaction of thiacyclobutane with sulfuryl chloride.(132)

Treatment of thiacyclobutane with sulfuryl chloride gives a ring-opened compound, 3-chloropropanesulfenyl chloride.

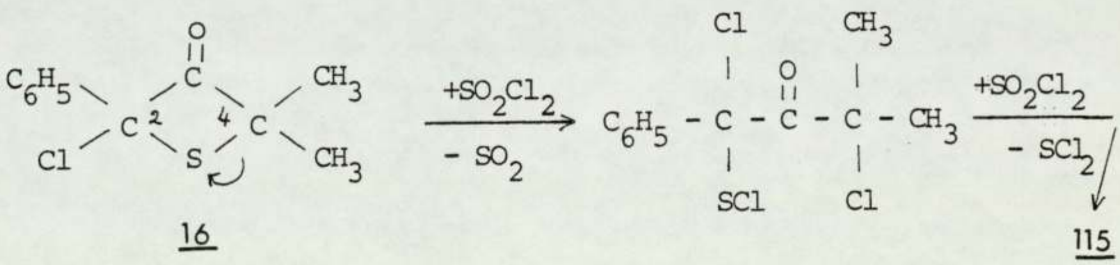


The reaction of chlorothietanone 16 probably proceeds via an initial carbon-sulfur cleavage followed by elimination of sulfur dichloride and then chlorination occurs on carbon-2. There are two pathways for carbon-sulfur bond cleavage, i.e. scheme a or b.

Scheme a:



Scheme b:



Several workers (133) have studied the position of chlorination. They have found the position at which chlorination occurs depends mainly on the stability of the carbon radical or carbocation $(\dot{R},\overset{+}{R})$ formed, but some steric or solvent effects may also be involved. The tertiary hydrogen can more easily be substituted because the tertiary carbon radical formed is more stable than the primary one.

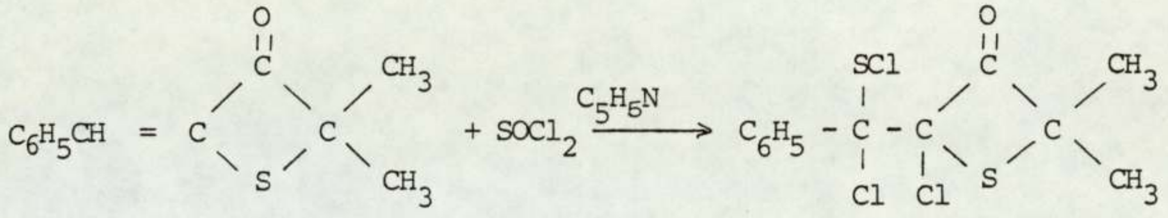
An electron-withdrawing group destabilizes the adjacent carbon radical, and free radical chlorination is favoured on the carbon atom remote from the electron-withdrawing group. Some typical examples of product distributions of the chlorination of the hydrocarbons having electron withdrawing groups with sulfuryl chloride are shown:

Substrate	α-Cl	β-Cl	γ-Cl	δ-Cl
$ClCH_2-CH_2-CH_2CH_3$	7	23	46	24
$Cl_2CHCH_2CH_2CH_3$	2	13	48	37
$Cl_3CCH_2CH_2CH_3$	-	8	42	50

On these grounds, it is suggested the reaction proceeds via scheme b. The carbon-sulfur cleavage on carbon-4 is more favoured than carbon-2 because the carbocation of carbon-4 is more stable than carbon-2.

6 - d: α-Chloro-β-chloro-α-chlorosulfenylthietanone.

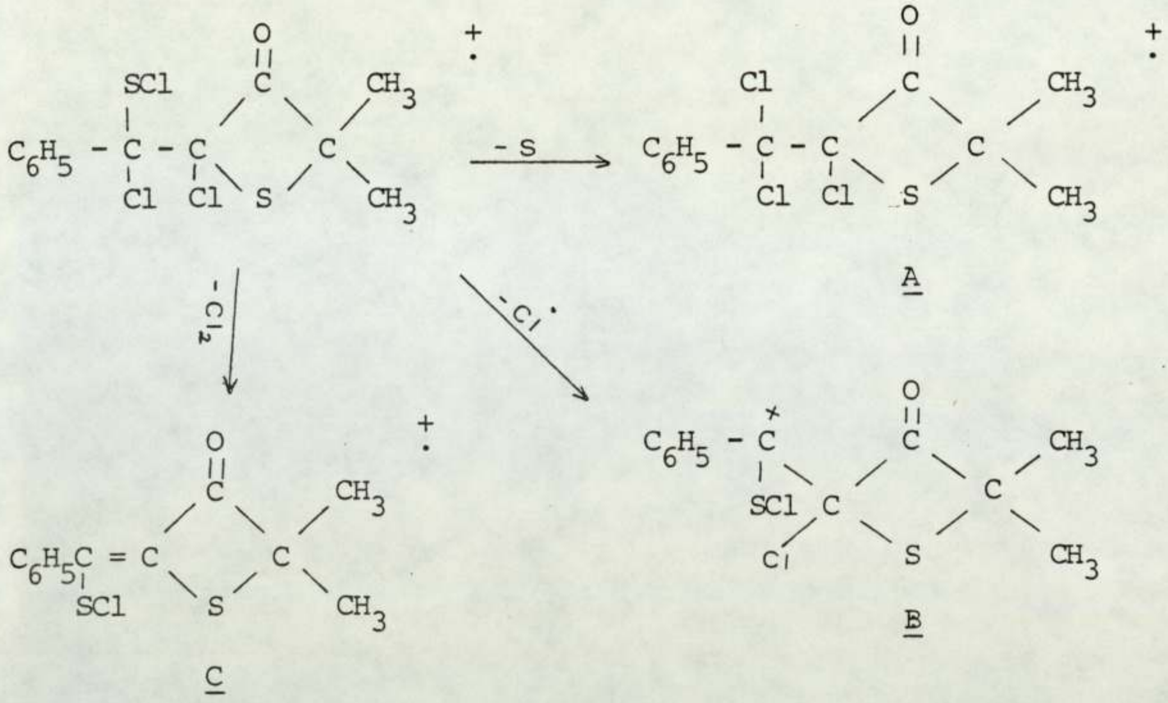
4-Benzylidene-2,2-dimethylthietan-3-one with thionyl chloride in the presence of pyridine gave an α-chloro-β-chloro-α-chlorosulfenyl adduct 116.



17

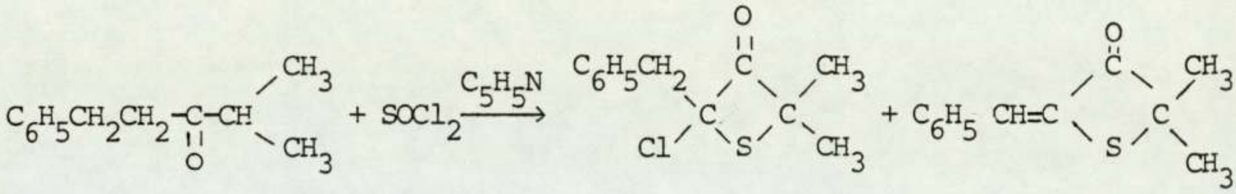
116

The disappearance of a peak at $1610cm^{-1}$ in the infrared spectrum showed the absence of the carbon-carbon double bond (C=C). A peak at $1780cm^{-1}$ was due to the carbonyl group. The position of the carbonyl group absorption confirmed the presence of a four-membered ring of the chlorothietanone. The carbonyl absorption of the thietanone B is shifted about $25cm^{-1}$ to a higher wave number when compared with the carbonyl absorption of the benzylidenethietanone. The conjugation effect in the benzylidenethietanone lowers the carbonyl wave number absorption and the inductive effect in the thietanone raises the carbonyl frequency. The nuclear magnetic resonance spectrum showed peaks at δ = 1.35, 1.85 and 7·65 ppm due to two methyl and phenyl groupsrespectively in relative intensities of 3:3:5. The mass spectrum of the product showed a parent ion peak at 340 mass unit. The value of the mass of the molecular ion was of great help in identifying the structure of the product. The peaks at 308, 305 and 270 mass units are due to fragment ions A, B and C.



The loss of sulfur (S), chlorine atom and sulfenyl chloride (S–Cl) are favourable processes. The resulting M-S peak is more intense than the molecular ion. The accurate mass spectrum of ions at $\frac{m}{e}$ 340 and 308 gave molecular formulas $C_{12}H_{11}Cl_3OS_2$ and $C_{12}H_{11}Cl_3OS$ respectively. The presence of three chlorine atoms in the molecule was shown by measuring the relative intensity of peaks at M+2, M+4, M+6 and M+8 mass units.

Although the reaction of 2-methyl-5-phenylpentan-3-one with thionyl chloride gave the mixture of the thietanones 17, 116, 117, 118 when refluxed for a long time, it was not possible to separate the mixture by physical methods.



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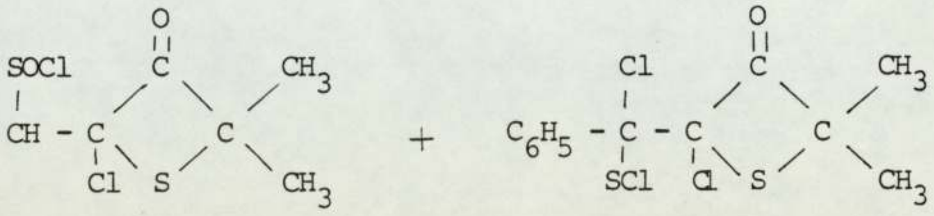
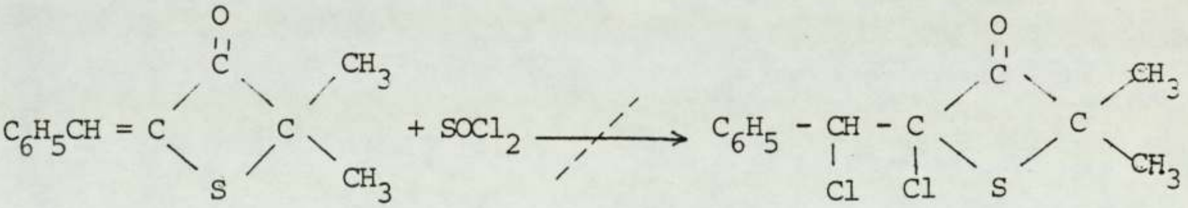


118

116

2-Methyl-5-phenylpentan-3-one on treatment with thionyl chloride can give a variety of products 17, 116, 117 or 118 depending on the applied conditions. Pizey et al.(19) have reported the benzylidenethietanone 17 on treatment with thionyl chloride gives the dichloro-adduct 119.



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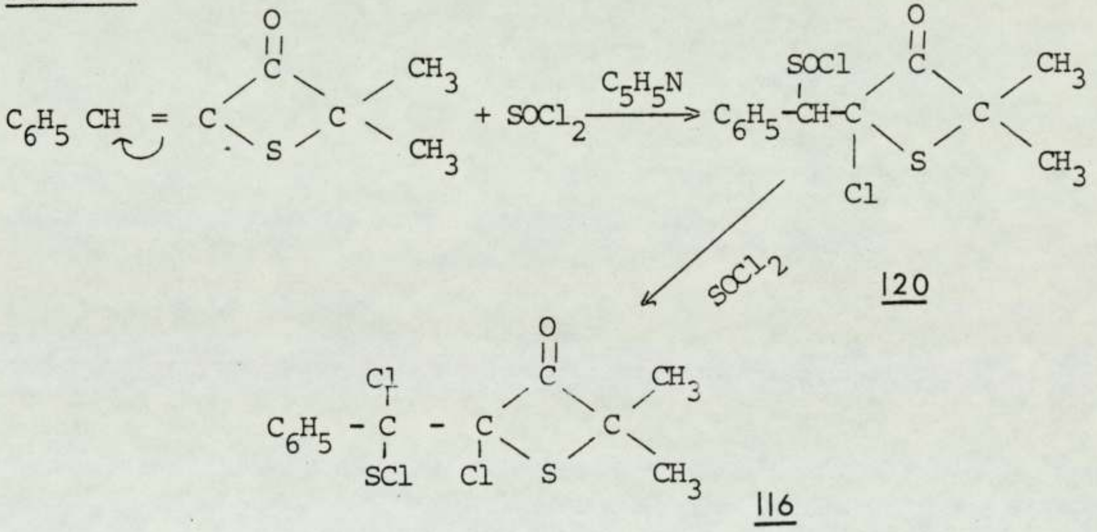
119

We have shown that the dichlorothietanone 119 was not formed in this reaction under the same conditions. In fact the spectroscopy data given by the authors do not agree with structure 119. According to compound 119, the methine proton should appear at about δ = 5-6ppm. The absence of a methine proton at this position in the NMR spectrum, and the presence of a parent ion peak at 340 mass units are good evidence that the product is not the dichlorothietanone 119.

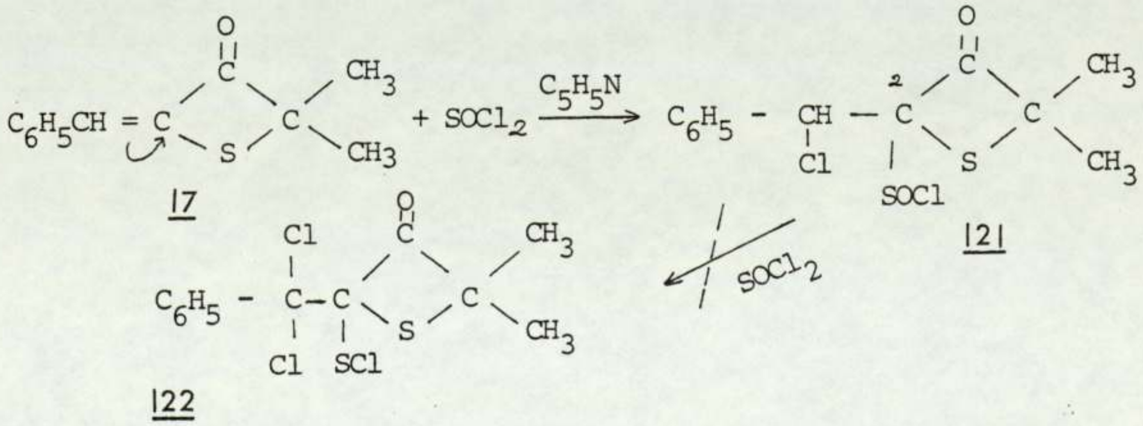
Furthermore, the fragments B and C in the mass spectrum and S-Cl stretching peak at 540cm^{-1} in the infrared spectrum reveal the formation of 116 rather than 119.

The initial step of the reaction of 4-benzylidene-2,2-dimethylthietan-3-one with thionyl chloride is an electrophilic addition of thionyl chloride across the double bond of the benzylidenethietanone 17 to form sulfinyl chloride 120 which is then converted to the 4-chloro-α-chloro-α-chlorosulfenyl 116 by the Pummerer reaction.

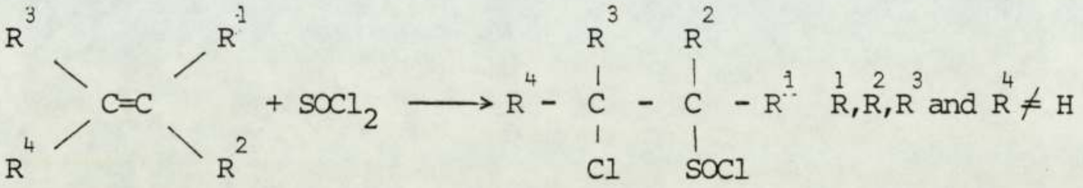
Scheme a:



This addition agrees with the empirical generalisation of Markownikov. If anti-Markownikov addition occurs the product should be the β-chloro-αchlorosulfinylthietanone 121.



It is unlikely that thietanone 121 with excess thionyl chloride formed the thietanone 122 The absence of a proton joined to the sulfinyl chloride (C-2) stops further reaction with excess thionyl chloride to form 122, e.g. the unsaturated 123 with thionyl chloride in the presence of pyridine gives the sulfinyl chloride 124 (25)

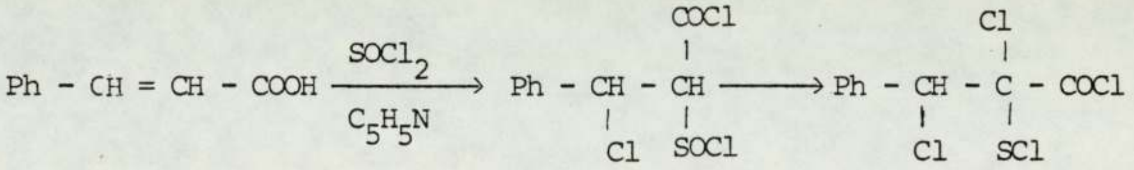


123

124

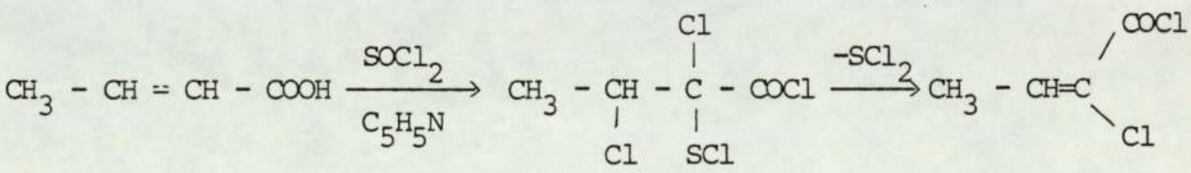
Further evidence which supports the reaction proceeding by scheme a and the product being 4-chloro-α-chloro-α-chlorosulfenyl compound 116 is:

Treatment of the unsaturated cinnamic acid and trans-crotonic acid with excess of thionyl chloride (7 equiv.) in the presence of pyridine gives the α-chloro-α-chlorosulfenyl acid chloride 125. (105)



$$Ph-CH=CH-COOH \xrightarrow[C_5H_5N]{SOCl_2} Ph-\underset{Cl}{CH}-\underset{SOCl}{\overset{COCl}{CH}} \longrightarrow Ph-\underset{Cl}{CH}-\underset{SCl}{\overset{Cl}{C}}-COCl$$

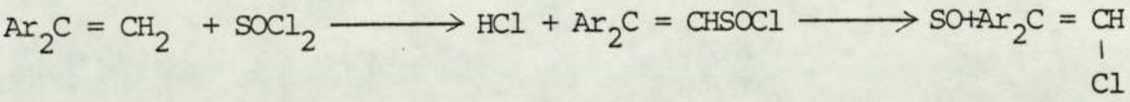
125



$$CH_3-CH=CH-COOH \xrightarrow[C_5H_5N]{SOCl_2} CH_3-\underset{Cl}{CH}-\underset{SCl}{\overset{Cl}{C}}-COCl \xrightarrow{-SCl_2} CH_3-CH{=}C\begin{matrix}COCl\\Cl\end{matrix}$$

6 - e: Comment on the article of Patai (26, 27) about the reaction between unsaturated compound and thionyl chloride .

1,1-Diphenylethylene 29 on treatment with thionyl chloride was reported (26, 27) to give 1,1-diphenylethylene-2-sulfinyl chloride 126 in 17% yield and the main reaction product was 1,1-diarylvinyl-chloride 30, e.g.

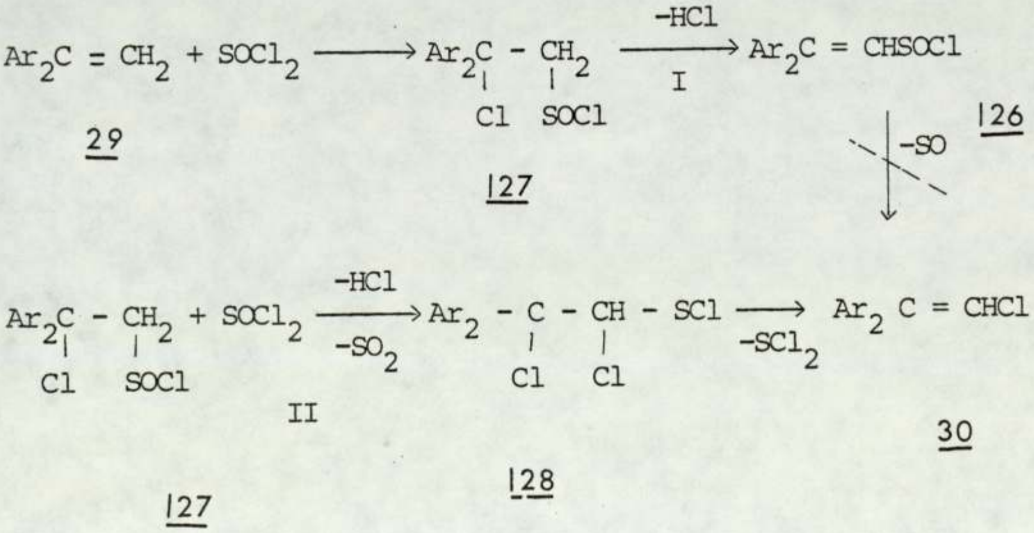


$$Ar_2C = CH_2 + SOCl_2 \longrightarrow HCl + Ar_2C = CHSOCl \longrightarrow SO + Ar_2C = \underset{\displaystyle Cl}{\underset{|}{CH}}$$

29 126 30

Patai (26,27) suggested the reaction intermediate is the sulfinyl chloride 126 which loses sulfur monoxide (SO) to give 30.
This seems rather unlikely, since the loss of sulfur monoxide (SO) should not easily occur. According to our work and that of Higa (105) we suggest the mechanism of this reaction could follow scheme a.

Scheme a:



$$Ar_2C = CH_2 + SOCl_2 \longrightarrow Ar_2\underset{\displaystyle Cl}{\underset{|}{C}} - \underset{\displaystyle SOCl}{\underset{|}{CH_2}} \xrightarrow[I]{-HCl} Ar_2C = CHSOCl \;\; \cancel{\downarrow -SO}$$

$$Ar_2\underset{\displaystyle Cl}{\underset{|}{C}} - \underset{\displaystyle SOCl}{\underset{|}{CH_2}} + SOCl_2 \xrightarrow[-SO_2]{-HCl} Ar_2 - \underset{\displaystyle Cl}{\underset{|}{C}} - \underset{\displaystyle Cl}{\underset{|}{CH}} - SCl \xrightarrow[-SCl_2]{} Ar_2\,C = CHCl$$

The first stage is the formation of the α-chloro-β-chlorosulfinyl compound 127. The α-chloro-β-chlorosulfinyl 127 may then undergo either pathway I or pathway II.

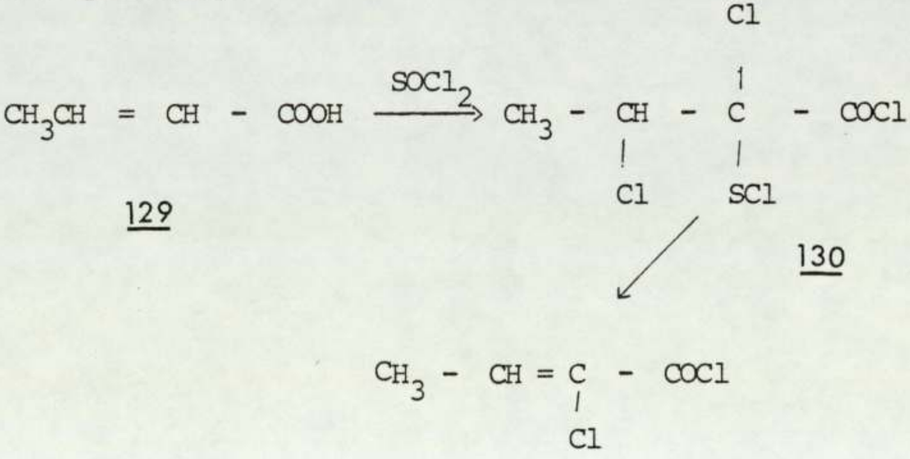
I : The chloro-sulfinyl chloride 127 can lose hydrochloric acid to give 126.

II: The chloro-sulfinyl chloride 127 with excess thionyl chloride can give α-chloro-β-chlorosulfenyl compound 128 which then gives the chloro-compound 30.

The evidence to support the formation of 128 in the above reaction is:

1 - The 4-chloro-α-chloro-α-chlorosulfenyl 116 was isolated from the reaction of 4-benzylidene-2,2-dimethylthietan-3-one with thionyl chloride.

2 - Higa (105) has studied the reaction of *trans*-crotonic acid 129 with excess of thionyl chloride in the presence of pyridine. Fractional distillation of the mixture furnished α-chlorosulfenylbutanoyl chloride 130 and 2-chloro-2-butenoyl chloride 131 in 55% and 10% yield respectively.



$$CH_3CH = CH - COOH \xrightarrow{SOCl_2} CH_3 - \underset{Cl}{CH} - \overset{Cl}{\underset{SCl}{C}} - COCl$$

129 130

$$CH_3 - CH = \underset{Cl}{C} - COCl$$

131

CONCLUSIONS

The work presented in this thesis consists of a study of the physical and chemical properties of β-ketosulfinyl chlorides, ketosulfenylchlorides and thietan-3-ones. The chemical behaviour of the ketosulfinyl chlorides on treatment with bases, pyridine and triethylamine indicates that they lose hydrochloric acid, but the product is not the thietan-3-one 1-oxide.

It was found that β-ketosulfinyl chlorides containing one α-proton (methine joined to the sulfinyl chloride group) on treatment with thionyl chloride gave the α-chloro-β-keto-α-sulfenyl chloride.
The sulfenyl chlorides were shown to be formed from the reaction between certain ketones with sulfur dichloride in the presence of pyridine or aluminium chloride depending on the nature of the ketone.

The formation of thietan-3-ones was an interesting aspect of this work; sulfinyl chlorides or chlorosulfenyl chlorides were found to be intermediates in the cyclisation of the ketones by treatment with thionyl chlorides. The planarity of the thietanones was determined by nuclear magnetic resonance phenomena. The strain in the four membered rings of the thietanones was rationalized in terms of physical and chemical properties. The synthesis of the thietanone 1-oxide was attempted in order to study the mechanism of the reaction of certain ketones with thionyl chloride. The reaction of the chlorothietanones with various reagents (nucleophiles, reducing and chlorinating reagents) has been studied. When 2-chlorothietanones are treated with piperidine, morpholine, pyrrolidine, methanol and benzylmercaptan as nucleophiles, these nucleophiles tend to substitute on the C-2 of the 2-chlorothietanones.

The 2-chlorothietanones on treatment with hydrazine derivatives have been attacked at both the C-2 and C-3 of the thietanone. From the nucleophilic reaction it was concluded that the C-2 has sp^2 characteristics. It was shown that the reaction of an unsaturated thietanone with thionyl chloride was by an electrophilic addition.

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