A STUDY OF THE REACTIONS BETWEEN SULPHUR HALIDES AND OXYHALIDES WITH COMPOUNDS CONTAINING ACTIVE METHYLENE GROUPS

by

CLIFFORD JAMES IRELAND

A Thesis submitted for the Degree of Doctor of Philosophy of The University of Aston in Birmingham

May 1973

546.22 IRE 27 June 73.163197.

#### SUMMARY

A series of reactions of thionyl chloride with compounds containing active methylene groups has led to a new synthesis of tetrasubstituted alkenes. The synthesis employs cheap and readily available starting materials, and leads to good yields of alkenes in a simple one-stage process.

The study has been divided into two main parts, the first being an investigation of the reaction of thionyl chloride with a number of compounds containing carbon-hydrogen bonds labilised by the presence of adjacent electron-withdrawing groups. Hence, some idea of the scope and utility of the new synthesis has been obtained.

The second part of the study has been devoted to the determination of a reaction mechanism or mechanisms. It is shown that a sulphinyl chloride is formed by an ionic route and in most cases is unstable under the reaction conditions. Loss of hydrogen chloride from the sulphinyl chloride leads to a sulphine which in turn yields an alkene via an intermediate thiiran.

Not every reaction yields an alkene, however, and in certain cases the intermediates postulated in the alkene synthesis are too stable to react further with thionyl chloride. This results in a sulphinyl chloride and two thiirans being isolated as major products.

An attempt has been made to explain the formation of di(acetylalkoxycarbonyl)methyl sulphide from the reaction of acetoacetic esters and thionyl chloride at room temperature. It is thought that a different pathway is followed owing to the reaction of the thionyl chloride with the enolic tautomer rather than with a carbanionic-type species.

Both sulphuryl chloride and disulphur dichloride have been used to prepare compounds by known routes. The products of these reactions

i

are compared with those from certain thionyl chloride reactions in order to verify particular structures.

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This work was carried out between 1969 and 1972 in the University of Aston in Birmingham. It has been done independently and has not been submitted for any other degree.

C.J. Ireland 8th May 1973

## Acknowledgments

I would like to express my sincere thanks to Mr. J.S. Pizey for his constant advice and encouragement throughout the progress of this work.

I am also indebted to the following laboratory staff for the instrumental analyses; Mrs. V.M. Clenton for i.r. spectra, Mrs. B.W. Evans for gas chromatography, Mr. E.J. Hartland for n.m.r. spectra and Mr M.J. Houghton for mass spectra.

My thanks also go to my wife, Sue, who expertly typed the manuscript.

Finally, I would like to thank the Science Research Council for their financial support of this work.

	CONTENTS	Page
	SUMMARY	i
Chapter 1	INTRODUCTION	1
Chapter 2	SYNTHETIC EXPERIMENTAL PROCEDURES	12
2.1	Introduction	12
2.2	Instrumental Analysis	12
2.3.	Reagents, Solvents and Apparatus	13
2.4	Reactions of Thionyl Chloride	13
2.4.1	Preparation of Tetra-substituted Alkenes	13
2.4.2	Preparation of Di(acetylalkoxycarbonyl)methyl	
	sulphides	17
2.4.3	Preparation of Sulphinyl Chlorides and Thiirans	19
2.4.4	The Reactions of Thionyl Chloride with a	
	Miscellaneous Group of Compounds	22
2.4.5	The Action of Thionyl Chloride on ~-Alkyl	
	substituted Compounds	23
2.4.6	The Action of Thionyl Chloride on Proposed	
	Intermediates	25
2.5	Reactions of Disulphur Dichloride (S2Cl2)	26
2.5.1	Preparation of Tetra-substituted Alkenes	27
2.5.2	Reaction with Dimethyl Malonate	27
2.5.3	Preparation of Sulphides	28
2.6.	Reactions of Sulphuryl Chloride (S02C12)	29
2.7	Preparation of ~-alkyl substituted compounds	29
2.8.	Preparation of Esters	31
2.9	Preparation of Sulphinyl Chlorides	33
2.10	Preparation of Thiirans	34
2.11	Preparation of Thiols and Disulphides	36
2.12	Preparation of Other Compounds	38
2.13	Attempted preparation of Di(acetylethoxycarbonyl)-	
Str. High	methyl sulphoxide	39

v

		Page
Chapter 3	MECHANISTIC EXPERIMENTAL PROCEDURES	42
3.1	Introduction	42
3.2	Gas Evolution Studies	42
3.2.1	Experimental Details of the Sulphur Dioxide	
	Evolution Study	42
3.2.2	Experimental Details of the Hydrogen Chloride	
	Evolution Study	43
3.2.3	Results	45
3.3	The Reaction between Diethyl malonate and a mixture	
	of Disulphur dichloride and Sulphuryl chloride	46
3.4	The Attempted 'Trapping' of a Carbanion Intermediate	47
3.5	The Attempted 'Trapping' of a Sulphine Intermediate	50
3.6	The Attempted Preparation of a 'Cross-product'	51
3.7	The Reaction of Ethyl Cyanoacetate and Thionyl	
	Chloride Studied by N.M.R. Spectrometry	52
3.8	The Detection of Diethyl Dicyanomaleate	52
Chapter 4	DISCUSSION OF SYNTHETIC EXPERIMENTAL RESULTS	55
Chapter 5	DISCUSSION OF MECHANISTIC EXPERIMENTAL RESULTS	70
5.1	A General Reaction Mechanism	70
5.2	The Feasibility of a Free-Radical Reaction Mechanism	90
5.3	Discussion of Gas Evolution Experiments	96
5.4	Stereochemical Consideration of the Formation of	
	Alkenes using Thionyl Chloride Reagent	99
Chapter 6	CONCLUSION	111
	APPENDIX I	113
	APPENDIX II	114
	REFERENCES	115

vi

# LIST OF FIGURES

Fig.	1	Mass Spectrum of Diethyl Dicyanofumarate	between	p.	14	and	15
Fig.	2 .	Mass Spectrum of Tetramethoxycarbonyl-					
		ethene	between	p.	15	and	16
Fig.	3	Mass Spectrum of Tetramethyl 1,2,4,5-					
		tetrathian-3,3,6,6-tetracarboxylate	between	p.	28	and	29
Fig.	4	Gas Evolution Apparatus	between	p.	42	and	43
Fig.	5	Plot of (Weight of sulphur dioxide) against					
		Time	between	p.	46	and	47
Fig.	6	Plot of (Weight of sulphur dioxide) against					
		Time	between	p.	46	and	47
Fig.	7	Plot of $1/(a-x)^{\frac{1}{2}}$ against Time	between	p.	46	and	47
Fig.	8	Plot of 1/(a-x) against Time	between	p.	46	and	47
Fig.	9	Concentration of Intermediate in					
		Consecutive Reactions	between	p.	81	and	82

# LIST OF TABLES

Table 1	The Keto-enol Contents and pK Values of					
	Some Selected Compounds			p	. 9	
Table 2	Products obtained from the Reaction of					
	Diethyl malonate (0.1 mole) with a mixture					
	of Disulphur dichloride and Sulphuryl					
	chloride			p.	47	
Table 3	The Reaction Products of SOC12 and X-CH2-Y			p.	55	
Table 4	Principle Stable Heavier Isotopes			p.	57	
Table 5	Mass Spectrum of Diethyl Dicyanofumarate	between	p.	58	and	59
Table 6	Mass Spectrum of Tetramethoxycarbonyl-					
	ethene	between	p.	58	and	59
Table 7	Mass Spectrum of Tetramethyl 1,2,4,5-tetra-					
	thian-3,3,6,6-tetracarboxylate	between	p.	58	and	59

#### Chapter 1

#### INTRODUCTION

The synthetic uses of thionyl chloride have been appreciated for many years, and numerous reviews and articles have been published dealing with its general reactions<sup>1,2</sup> and its uses in organic synthesis<sup>3,4</sup>. As the field has been thoroughly covered no attempt will be made here to give a complete review, but it is felt that a brief survey of the general classes of reactions is in order.

The reaction with an alcohol to yield a chloride has probably been most exhaustively studied, and it has been found to occur with retention of configuration, partial or complete inversion of configuration, or accompanied by a molecular rearrangement.

The first case is an example of an  $S_N$ i mechanism, where the intermediate alkyl chlorosulphite dissociates into an intimate ion pair and, simultaneously, the chlorine atom of the leaving group attacks the carbon atom next to the oxygen.

$$\operatorname{ROH} + \operatorname{SOCl}_2 \xrightarrow{-\operatorname{HCl}} \operatorname{R-O-S=0} \xrightarrow{\operatorname{R-I}} \operatorname{R-O-S=0} \xrightarrow{\operatorname{RCl}} \operatorname{RCl} + \operatorname{SO}_2$$

(Throughout this thesis,  $R = alkyl and Ph = phenyl C_6H_5$ )

In the presence of a base, such as pyridine, the backside attack by the formed chloride ion on the alkyl chlorosulphite is favoured, and inversion of configuration may occur.

An  $S_N^2$  mechanism would favour complete inversion of configuration,

whereas the  $\mathrm{S}_{\mathrm{N}}^{}1$  mode of attack would result in racemisation of the product.

. The treatment of a secondary aliphatic alcohol with thionyl chloride may result in a tertiary alkyl chloride.

Under carefully controlled conditions two further products may be obtained from the reaction of alcohols with thionyl chloride. In the absence of any base and with a constant stream of carbon dioxide passing through the reaction mixture, the alkyl chlorosulphite is stable and can be distilled off. If a base is present and a solvent in which hydrogen chloride is insoluble is used, a dialkyl sulphite is formed in good yield. An interesting example of cyclic sulphite formation occurs in the reaction between thionyl chloride and certain diols.

e.g.

 $\begin{array}{c} \overset{\mathrm{CH}_{2}\mathrm{OH}}{|}_{\mathrm{CH}_{2}\mathrm{OH}} + \operatorname{Socl}_{2} \longrightarrow \begin{array}{c} \overset{\mathrm{CH}_{2}\mathrm{-0}}{|}_{\mathrm{CH}_{2}\mathrm{-0}} \end{array} \\ \overset{\mathrm{CH}_{2}\mathrm{OH}}{|}_{\mathrm{CH}_{2}\mathrm{OH}} \end{array}$ 

The reaction of a carboxylic acid with thionyl chloride is, in some ways, similar to that with alcohols. Many acids react directly with thionyl chloride to give an acid chloride, RCOC1, however some acids do not react at all while others only give anhydrides<sup>5</sup>. Carré and Libermann<sup>6</sup> noted that if the reaction was base catalysed, then previously unreactive and anhydride-forming acids could be made to yield acid chlorides. An anhydride is formed as an intermediate but is attacked in a slow step by another molecule of thionyl chloride to give the acid chloride. This reaction was used in a recent paper on the synthesis of anhydrides of monobasic acids using equimolar quantities of acid and thionyl chloride<sup>7</sup>.

-2-

Thionyl chloride may be used to prepare sulphinyl and sulphonyl chlorides from the corresponding acids.

An interesting paper describes the preparation of *<*-chloro-*<*-sulphenyl-4-nitro-2,5-dimethoxyphenylacetyl chloride from 4-nitro-2,5-dimethoxyphenylacetic acid and excess thionyl chloride in the presence of pyridine<sup>8</sup>.



A more recent study<sup>9</sup> showed that oxidation of a methylene adjacent to a carbonyl group is not as unusual as at first thought and involves a Hell-Volhard-Zelinsky type addition followed by a Pummerer rearrangement<sup>19</sup>.





A similar mechanism has been proposed<sup>10</sup> for the initial reaction of 4-phenylbutan-2-one with thionyl chloride to give the unusual compound, 2-benzylidenethietan-3-one.

$$\begin{array}{ccccccc} \text{PhCH}_2\text{CH}_2\text{CCH}_3 + \text{SOCl}_2 & \xrightarrow{\text{C}_5\text{H}_5\text{N}} \text{PhCH}_2\text{CCOCH}_3 & \xrightarrow{\text{Cl}} \text{PhCH}_2\text{CC-C=CH}_2 \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ \end{array}$$

Groups derived from carboxylic acids are usually unreactive towards thionyl chloride, a fact borne out by the work completed on esters and nitriles in this thesis. Acid chlorides have been formed by prolonged treatment of esters with thionyl chloride<sup>11</sup> and this compares well with our own finding that ethyl phenylacetate gives a low yield of diphenylmaleic anhydride under similar conditions.

Nitriles do not usually react with thionyl chloride, an observation easily verified by noting that thionyl chloride is used to prepare nitriles from amides.

$$RCONH_2 + SOC1_2 \longrightarrow RCN + SO_2 + 2HC1_2$$

Diphenylacetamide, when heated under reflux for six hours with thionyl chloride, yields diphenylacetonitrile<sup>12</sup> but longer treatment produces the chlorinated product, chlorodiphenylacetonitrile.

Thionyl chloride can add directly across alkene linkages to give sulphinyl chlorides and sulphoxides or sulphides. Both 1-chlorosulphinyl-2-chloroethane and bis (2-chloroethyl) sulphide have been obtained from the reaction of thionyl chloride with ethylene<sup>13</sup>. Similar types of products are obtained when the reacting species is an

-4-

enol ether<sup>14</sup>, i.e.





An interesting isomerisation has been recorded in which catalytic quantities of thionyl chloride were used to convert dimethyl maleate to dimethyl fumarate in high yield<sup>15</sup>. The usual inert character of alkenes towards thionyl chloride is demonstrated in the preparation of alkenes from the appropriate alcohol by dehydration using thionyl chloride.



One early source of interest in thicnyl chloride chemistry was its reaction with phenols. Under controlled conditions the products obtained are the aryl chlorosulphite and diaryl sulphite<sup>16</sup>, a reaction analagous to that of alcohols.



A more common reaction of phenols with thionyl chloride involves the use of a catalyst (usually copper), the product then being a diaryl sulphide. Sulphoxides are not usually obtained as they are easily

-5-

reduced by thionyl chloride<sup>17</sup>. However, there are exceptions, for example azulene affords di-1-azulyl sulphoxide<sup>18</sup>.



If the sulphoxide possesses an  $\propto$ -carbon atom carrying a replaceable hydrogen atom, then the presence of thicnyl chloride causes a Pummerer rearrangement<sup>19</sup> and an  $\propto$ -chlorosulphide results<sup>20</sup>.

$$\begin{array}{c} \operatorname{Ph-S-Me} + \operatorname{SOCl}_{2} \longrightarrow \begin{bmatrix} \operatorname{Ph-S-Me} \\ 0 \\ 0 \\ -\operatorname{S-Cl} \end{bmatrix}^{+} \operatorname{Cl}^{-} \xrightarrow{-\operatorname{SO}_{2}} \begin{bmatrix} \operatorname{Ph-S-Me} \\ 1 \\ -\operatorname{Cl} \end{bmatrix}^{+} \operatorname{Cl}^{-} \\ \begin{array}{c} -\operatorname{SO}_{2} \\ -\operatorname{S-CH}_{2} \end{bmatrix}^{+} \operatorname{Cl}^{-} \\ \end{array}$$

Similar results have been obtained by Russell et al, although in one instance the chlorination of an  $\ll$ -methyl- $\beta$ -ketosulphoxide produced an  $\ll$ -chloromethyl- $\beta$ -ketosulphide<sup>21</sup>.



The preparation of heterocyclic sulphur compounds has recently become a useful synthetic route although in most cases the discovery was initially accidental. Goldman has developed a synthesis of 4,5,6,7-tetrahydrothiazolo [4,5-d] pyrimidine-5,7-diones by treating a

-6-

variety of 6-amino-1,3-dimethyluracils with thionyl chloride and pyridine<sup>22</sup>.





Davies and White also postulate a sulphinyl chloride intermediate losing hydrogen chloride to form a sulphine which undergoes a cyclisation reaction, affording 2,1-benzisothiazole from o-toluidine<sup>23</sup>.



A very simple route to thiophen-2,5-dicarbonylchloride from adipic acid has recently been published<sup>24</sup> but its full synthetic usefulness is only just beginning to be investigated<sup>25</sup>.



Thus from our knowledge of the chemistry of thionyl chloride it would appear reasonable to predict that ethyl acetoacetate and thionyl chloride would give the same product as that obtained from the action of phosphorus pentachloride on the  $\beta$ -ketoester<sup>26</sup>, namely 3-chlorocrotonoyl chloride. The hydroxyl group in the enolic form of ethyl acetoacetate should be replaceable by one chlorine atom and the ethoxy group by another.



## Keto

Enol

When the reaction was attempted the expected product was not obtained, but instead a white crystalline solid, di(acetylethoxycarbonyl)methyl sulphide, was formed. Hence further investigation was warranted. The sulphide was known and in fact had been made before by the same route<sup>27</sup>. However, there was no mention in this paper of the formation of ethyl <-chloroacetoacetate as a by-product. Methyl acetoacetate also yielded a sulphide and a chlorinated compound, and it was thought worthwhile to investigate the reaction further.

Acetoacetic esters are one of the most well-known groups of compounds to exhibit the property of keto-enol tautomerism, and thus it was thought possible that the reactivity towards thionyl chloride was due to an initial reaction with the enol tautomer, ethyl 3-hydroxycrotonate. A number of different compounds were investigated on the basis of their reported enol composition and carbon-acid strengths (Table 1). Those compounds possessing a high percentage of

-8-

Table 1.	The	keto-enol	contents	and	pKa	values	of	some	selected
	com	pounds.							

Formula of Compound	Enol Content(%)		pKa*	
	Ref. 31	Ref. 32	Ref. 33	
CH3COCH2C02Me		0	10	
CH <sub>2</sub> COCH <sub>2</sub> CO <sub>2</sub> Et	8	8		11 <sup>34</sup>
CH <sub>3</sub> COCHCO <sub>2</sub> Et Me		5		
CH3COCH2COCH3	76.4	81	9	
сн <sub>3</sub> соснсосн <sub>3</sub> сн <sub>3</sub>		30	11	
CNCH2C02Et	$2.5 \times 10^{-1}$		9	
CH <sub>2</sub> (CO <sub>2</sub> Et) <sub>2</sub>	$7.7 \times 10^{-3}$		13.5	Section Section
EtCH(CO2Et)2			15	
CH <sub>2</sub> Ph <sub>2</sub>	an a		•	35 <sup>35</sup>
PhCOCH2C02Et	17.7	22		
PhCOCH	$3.5 \times 10^{-2}$		Set 1	19 <sup>34</sup>
PhCOCH <sub>2</sub> Me	$1.0 \times 10^{-2}$			
(CH <sub>2</sub> ) <sub>5</sub> CO	1.2			
CH3COCOCH3	1.1			
CH3COCH2COPh	89.2	100	9.5	and the second
PhCOCH <sub>2</sub> COPh		100		
Fluorene				2535
CH2(CN)2			11	11 <sup>34</sup>
CH <sub>3</sub> CO <sub>2</sub> Et			24.5	

\* The effectiveness of unsaturated functional groups on the  $pK_a$  value<sup>34</sup> of a parent compound is in the order,  $-NO_2 > -COR > -SO_2R > -CO_2R$  and -CN > -SOR > Ph. Acidity is increased (about  $2pK_a$  units) by a chlorine or bromine substituent and decreased (1 to 2  $pK_a$  units) by an alkyl substituent.

-9-

enolic character gave complex or intractable reaction products on treatment with thionyl chloride, whereas compounds with less than 1% enol character, but significant carbon-acid strength, often yielded the corresponding tetra-substituted alkene.

 $2 \xrightarrow{X} CH_2 + 2SOC1_2 \longrightarrow \xrightarrow{X} Y + SO_2 + S + 4HC1$ 

(The nature of the groups X and Y are shown in Table 3)

Alkenes may be prepared by several routes, e.g. by the dehydration of primary alcohols, the dehydrohalogenation of alkyl halides or by the Wittig reaction of aldehydes and ketones. None of these methods provides a satisfactory route to a tetra-substituted product and it was thought worthwhile investigating the full potential of a method using thionyl chloride. The reaction's simplicity lends itself to further use in organic synthesis. Naik reported that tetraethoxycarbonylethene was obtained from the action of disulphur dichloride on diethyl malonate<sup>28</sup> while Cairns used the same reagent for a preparation of tetracyanoethylene<sup>29</sup>. Disulphur dichloride does not seem to have found any widespread application in this field however. Recently<sup>30</sup>, a twofold extrusion process was used for an alkene synthesis whereby a cyclic compound was prepared initially and heated with an alkyl or aryl phosphine, e.g.



It is thought that a thiiran is probably formed in an intermediate step.

Having ascertained that thionyl chloride is an efficient reagent for the preparation of alkenes it became necessary to investigate the mechanism of the reaction. It was not necessary to use a compound exhibiting keto-enol tautomerism for the preparation of an alkene since both malononitrile and phenylacetonitrile yielded alkenes on treatment with thionyl chloride. The formation of a carbanion seemed the most likely first step although the possibility of a free-radical mechanism could obviously not be dismissed.

A detailed discussion of the various alternative mechanisms may be found in Chapter 5.

#### Chapter 2

#### SYNTHETIC EXPERIMENTAL PROCEDURES

#### 2.1. Introduction

This chapter incorporates the experimental details of the preparative chemistry in this thesis. A number of experiments, designed to assist in the elucidation of the mechanism, are not included here but are described in Chapter 3.

It is difficult to arrange a synthetic experimental chapter in a logical sequence because of the individual nature of each experiment. In an attempt to establish a meaningful order, the work has been classified into different types of reactions. The reactions of thionyl chloride, disulphur dichloride and sulphuryl chloride are under separate headings as are the preparations and attempted preparations of a variety of miscellaneous compounds.

#### 2.2. Instrumental Analysis

Infrared spectra were recorded on a Perkin-Elmer 237 spectrometer. Perkin-Elmer R10(60 MHz) and R14 (100 MHz) spectrometers were used for the nuclear magnetic resonance spectra. In all cases tetramethylsilane was used as an internal standard and its position marked at  $\tau$ 10.0. Mass spectra were obtained using an AEI MS9 mass spectrometer. Gasliquid chromatograms were run on a Pye Panchromatograph with a flameionisation detector. The column was usually carbowax 20M on Universal B support (60/85 mesh) but for higher temperatures (up to 250°C) Siliconegum on Firebrick (60/80 mesh) was used. All melting points are uncorrected.

<u>Units</u>. The units quoted are those in normal usage. In accordance with SI units, however, the relationship between millimetres of mercury (mmHg) and newtons per square metre (N  $m^{-2}$ ) is,

 $1 \text{ mmHg} = 13.595 \text{ x } 980.665 \text{ x } 10^{-2} \text{ N m}^{-2}$ 

-12-

#### 2.3. Reagents, Solvents and Apparatus

Unless otherwise stated, all the chemicals used were general purpose reagent (G.P.R.) grade. The solvents used in working-up procedures were also G.P.R. grade but those used for column and thinlayer chromatography were analytical reagent (A.R.) grade. Thionyl chloride (puriss A.R. grade) was obtained from Koch-Light Laboratories. No difference in the reaction with ethyl acetoacetate was observed when different grades of thionyl chloride were used. The same product and yield were obtained when G.P.R. grade, that distilled over quinoline, or a very pure form obtained using triphenyl phosphite<sup>36</sup> was used.

The apparatus for thionyl chloride experiments consisted of a round-bottomed flask attached to a reflux condenser with a calcium chloride drying-tube at the top. The contents of the flask were stirred magnetically.

## 2.4. Reactions of Thionyl Chloride

2.4.1. Preparation of Tetrasubstituted Alkenes

#### Preparation of Dimethyl dicyanofumarate

Methyl cyanoacetate (0.1 mole) was treated with thionyl chloride (0.13 mole) under reflux for three hours. The solution turned red initially and then black after fifteen minutes. After three hours, when no more hydrogen chloride or sulphur dioxide was evolved, the solution was allowed to cool to room temperature. The crystals, formed on standing, were filtered off through a sintered glass funnel and washed with cold ethanol. Sulphur formed as a solid lump at the bottom of the flask during the reaction and hence was easily separated from the organic product. The filtrate may be recrystallised from either acetone or petroleum ether (120-160°). White needles, m.p. 179-180°C. Yield 65-70%. (Found: C,49.3; H,3.07; N,14.8.  $C_8H_6N_2O_4$  requires C,49.5; H,3.09; N,14.4%).

n.m.r. (CDCl<sub>3</sub>): Singlet  $\tau$  5.95

-13-

i.r. (KBr disc): 3500(w), 2980(m), 2860(w), 1745(s), 1440(m), 1275(broad), 1015(m), 870(m), 760(m) cm<sup>-1</sup>.

#### Preparation of Diethyl dicyanofumarate

Ethyl cyanoacetate (0.1 mole) was treated with thionyl chloride (0.1 mole) under reflux for three hours. The solution turned red, then black after one hour. Crystals formed on cooling to room temperature and were filtered off, washed with cold ethanol and recrystallised from ethanol. White needles, m.p.  $115-6^{\circ}C$  (Lit.  $117^{\circ}C$ )<sup>37</sup>. Yield 65-70%. n.m.r. (CDCl<sub>3</sub>): Triplet  $\tau$  8.55 3 protons

Quartet 
$$\tau$$
 5.45 2 protons

i.r. (KBr disc): 2950(m), 1730(s), 1470(w), 1450(w), 1395(w), 1370(w), 1290(s), 1015(s), 850(m), 765(m) cm<sup>-1</sup>.

The mass spectrum of diethyl dicyanofumarate is given in Figure 1. Attempted preparation of Di-t-butyl dicyanofumarate

(1) t-Butyl cyanoacetate (0.1 mole) was treated with thionyl chloride (0.13 mole) under reflux for one hour by which time a viscous black tar was all that remained in the flask.

(2) Using the same proportions of reactants, the solution was stirred for twelve hours at room temperature. The solution turned black after fifteen minutes and there was a brisk evolution of gas. The mixture slowly solidified and all attempts at recrystallising the product were unsuccessful. In an effort to purify the black solid, it was dissolved in chloroform and passed down a silica-gel column by eluting with more chloroform. The resulting product was a brown solid with an indistinct melting point.

n.m.r. (CDCl<sub>3</sub>): Singlet τ 8.60 18 protons Singlet τ 8.30 9 protons Singlet τ 4.20 1 proton

#### Preparation of Tetramethoxycarbonylethene

Dimethyl malonate (0.1 mole) was treated with thionyl chloride

-14-



(0.13 mole) under reflux for four hours; by this time the reaction mixture had turned pale red. On cooling, white crystals formed which were filtered off from the red oil and sulphur, and recrystallised from ethanol. White needles, m.p.  $119-20^{\circ}$ C. (Lit.  $119-20^{\circ}$ C)<sup>38</sup>. Yield 55-60%. (Found: C,45.9; H,4.35. Calc. for C<sub>10</sub>H<sub>12</sub>O<sub>8</sub>: C,46.2; H,4.65%). n.m.r. (CDCl<sub>3</sub>): Singlet  $\tau$  6.12.

i.r. (KBr disc): 2960(m), 1735(s), 1442(s), 1430(m), 1250(s),

1040(m), 1025(s), 915(m), 870(m), 730(m), 725(m) cm<sup>-1</sup>.

The mass spectrum is given in Figure 2. Preparation of Tetraethoxycarbonylethene

Diethyl malonate (0.1 mole) was treated with thionyl chloride (0.13 mole) under reflux for six hours. After cooling the reaction product to  $-5^{\circ}C$  and leaving for several days, crystals slowly began to form in the yellow oil obtained. Rather than wait for such a slow process, a far more satisfactory procedure was to distil the oil under vacuum. It was necessary to use an air condenser to prevent the distillate solidifying and blocking the apparatus. The product crystallised in the receiving flask. Yield of oil distilling at  $155^{\circ}C$ (1.0 mmHg), 80-90%. The oily crystals may be recrystallised from petroleum ether (40-60°). A dilute solution must be used to stop the product reforming as an oil. White plates, m.p.  $50-51^{\circ}C$  (Lit.  $52-55^{\circ}C)^{39}$ .

n.m.r. (CDCl<sub>3</sub>): Triplet  $\tau$  8.70 3 protons Quartet  $\tau$  5.70 2 protons

i.r. (thin film): 2980(m), 2940(w), 2900(w), 1730(broad), 1470(m), 1445(m), 1370(s), 1240(broad), 1095(m), 1045(s), 860(m) cm<sup>-1</sup>.

Preparation of Tetraethoxycarbonylethene

Diethyl dicyanofumarate (4 g), ethanol (10 g) and concentrated sulphuric acid (8 g) were refluxed together for seven hours. The

-15-



resulting black solution was poured into 100 cm<sup>3</sup> of water and extracted with diethyl ether. The ethereal solution was dried with anhydrous magnesium sulphate and the ether was evaporated off to leave a dark brown oil. The oil was distilled under vacuum, b.p. 155°C (1.0 mmHg). Yield 35%. Analysis showed the product to be identical to that obtained from the reaction of diethyl malonate with thionyl chloride (see p. 15).

## Preparation of 1,2-Diphenylethene-1,2-dicarbonitrile

Phenylacetonitrile (0.1 mole) was treated with thionyl chloride (0.15 mole) under reflux in the presence of anhydrous aluminium chloride (0.05 g) for ninety-six hours, by which time the reaction mixture had become very dark brown. All remaining starting material was distilled off under reduced pressure (100-104°C, 1.0 mmHg) over an oil bath, leaving a black oil which was extracted with boiling petroleum ether (100-120°). Yellow crystals formed on cooling and were recrystallised from isopropanol. Pale yellow needles, m.p. 154-155°C (Lit. trans 161-2°C cis 134°C)<sup>40</sup>. Yield 22%. (Found: C,84.3; H,4.4; N,12.3. Calc. for  $C_{16}H_{10}N_2$ : C,83.5; H,4.4; N,12.2%). n.m.r. (CDCl<sub>3</sub>): Multiplet  $\tau$  1.90-2.30. i.r. (KBr disc): 2220(m), 1600(w), 1580(m), 1495(m), 1450(s), 1250(m),

1025(m), 1005(m), 820(m), 760(s), 695(s) cm<sup>-1</sup>.

## Preparation of Tetracyanoethylene

(1) Malononitrile (0.1 mole) was treated with thionyl chloride (0.13 mole) under reflux conditions. The solution immediately turned black and after fifteen minutes the reaction went out of control and a solid black mass was deposited on the inside of the condenser.

(2) Using the same proportions, the reaction was stirred at room temperature for twelve hours. The product was a solid black mass.

(3) In an attempt to slow down the reaction, several solvents were tried. In each case the reflux period was three hours.

-16-

- (a) Petroleum ether (60-80°). Product: a black solid
- (b) Benzene.
- (c) Benzene/Pet. ether (1:1). Product: a black solid
- (d) Benzene/Pet. ether (3:1). Product: a black solid
- (e) Benzene/Pet. ether (7:1). Product: a grey powder

No reaction

Reaction conditions (e) were used to obtain a product. The grey solid was ground up and heated to 100°C at 1.0 mmHg pressure in a sublimation apparatus. A yellow solid collected on the cold-finger. Yield 5%. i.r. (KBr disc): 2260(m), 2210(m), 1155(s), 1115(m), 1085(m), 960(s), 935(w), 915(w), 805(w) cm<sup>-1</sup>.

This agrees with the published data 41.

(4) The same conditions as in 3(e) were used except that the reaction was carried out under nitrogen to avoid any possibility of oxidation. No difference in the result was obtained.

# 2.4.2. Preparation of Di(acetylalkoxycarbonyl)methyl sulphides Preparation of Di(acetylethoxycarbonyl)methyl sulphide

A number of ratios of ethyl acetoacetate to thionyl chloride were tried so that an optimum yield might be obtained. The two liquids were stirred together at room temperature for sixteen hours. After four hours the solution turned brown and hydrogen chloride was evolved. The final reaction product appeared as a pale green solid mass which, on careful inspection, was seen to be composed of white crystals in a green liquid. The crystals were filtered off and recrystallised from ethanol. White needles, m.p. 115-6°C (Lit., 80-81°C<sup>42</sup>, 83-84°C<sup>43</sup>, 100-101°C<sup>27</sup>). (Found: C,50.0; H,6.3; S,12.2. Calc. for  $C_{12}H_{18}O_6S$ : C,49.6; H,6.3; S,11.0%).

n.m.r. (CCl<sub>4</sub>): Triplet  $\tau$  8.70 6 protons Singlet  $\tau$  7.60 6 protons Quartet  $\tau$  5.75 4 protons Singlet  $\tau$  -3.45 2 protons

-17-

i.r. (KBr): 2960(m), 2880(m), 2700(broad), 1750(w), 1600(broad), 1400(s), 1370(s), 1325(s), 1260(s), 1060(m), 1015(m), 960(m), 890(s), 855(m), 775(s) cm<sup>-1</sup>.

The green filtrate from the reaction mixture was distilled under vacuum to obtain all the volatile products. Maximum b.p. 52°C. (1.0 mmHg).

n.m.r. of distillate (CCl<sub>4</sub>): Triplet 
$$\tau 8.80^*$$
  
Triplet  $\tau 8.70^+$   
Singlet  $\tau 7.80^*$   
Singlet  $\tau 7.65^+$   
Singlet  $\tau 6.55^*$   
Quartet  $\tau 5.85^*$   
Quartet  $\tau 5.70^+$   
Singlet  $\tau 5.00^+$ 

\* Peaks attributable to ethyl acetoacetate

+ Peaks attributable to ethyl α-chloroacetoacetate

Batio of	% Yield (Calc. from wt. of ethyl acetoacetate)			
ethyl acetoacetate to thionyl chloride	Sulphide	Ethyl α-chloro- acetoacetate	Ethyl aceto- acetate	
1:1	29	30	10	
1.5:1	36		No. And State	
2:1	22	12	28	
2.25:1	25			
2.5:1	20			

Yield of products using different proportions of reactants.

The yield of sulphide could not be increased by increasing the reaction time or raising the temperature of the reaction. Both courses led to

-18-

charring of the product.

## Preparation of Di(acetylmethoxycarbonyl)methyl sulphide

Methyl acetoacetate (0.1 mole) was stirred with thionyl chloride (0.1 mole) at room temperature for sixteen hours. The solution turned red initially, but then changed to green. The crystals, which formed in the green solution when it was left for twenty-four hours, were filtered off and recrystallised from methanol. White needles, m.p.  $114-5^{\circ}$ C. Yield 21%. (Found: S,11.9.  $C_{10}H_{14}O_{6}S$  requires: S,12.2%).

n.m.r. (CCl<sub>4</sub>): Singlet  $\tau$  7.40 6 protons Singlet  $\tau$  6.05 6 protons Singlet  $\tau$  -3.60 2 protons

i.r. (KBr): 2950(m). 2700(broad), 1730(w), 1600(broad), 1440(s), 1370(s), 1340(s), 1250(s), 1060(m), 985(m), 880(s), 775(m) cm<sup>-1</sup>.

The green filtrate was distilled to give a liquid of b.p. 70-80°C. (15 mmHg). Yield 30%; n.m.r. showed that the distillate contained 55% methyl acetoacetate and 45% methyl  $\alpha$ -chloroacetoacetate. The n.m.r. spectrum of methyl  $\alpha$ -chloroacetoacetate (in CCl<sub>4</sub>) showed three singlets:  $\tau$ . 7.55 3 protons

τ 6.05 3 protons τ 4.95 1 proton

2.4.3. Preparation of Sulphinyl Chlorides and Thiirans Preparation of 2,3-Epithio-1,2,3,4-tetraphenylbutane-1,4-dione

Deoxybenzoin (0.1 mole) was treated with thionyl chloride (0.13 mole) under reflux for two hours. The reaction mixture gradually turned black during the first hour. After excess thionyl chloride had been removed under reduced pressure, the product was purified using column chromatography. A silica-gel column was used, through which the black oily product was eluted, first with carbon tetrachloride and then

-19-

with benzene. The silica-gel successfully removed all the black tar (which remained at the top of the column), and the major product obtained was a reddish-yellow oil which crystallised on standing to give long, oily yellow needles, recrystallised from petroleum ether ( $60-80^{\circ}$ ). m.p. 94-95°C. (Lit. trans 106-112°C, cis 174-5°C)<sup>44,45</sup>. n.m.r. (CDCl<sub>z</sub>): Multiplet  $\tau$  1.90-2.10

Multiplet 7 2.35-2.55

i.r. (KBr disc): 3070(s), 3040(m), 3010(w), 1660(s), 1600(s), 1580(s), 1455(s), 1330(m), 1320(m), 1295(m), 1215(s), 1180(m).

1165(m), 1000(s), 880(s), 795(s), 720(s), 700(s) cm<sup>-1</sup>.

The oily crystals obtained directly from the column had a similar spectrum, except that the peaks were more rounded because they were run as a thin film without any form of solvent.

Thin-layer chromatography was used to compare a sample from the reaction above with material obtained by a known route (p. 34). Separations were obtained using silica-gel spread on 20 cm. glass plates. The spots were developed by spraying the plates with a solution of iodine in chloroform. The results are in the table shown below.

		R <sub>f</sub> Values
Solvent	Product from PhCH_COPh + SOC1_2	Product from PhCH <sub>2</sub> COPh + MeC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> NSO
с <sub>6<sup>н</sup>6</sub>	0.75	0.75
<sup>C</sup> 6 <sup>H</sup> 6 <sup>/CC1</sup> 4 (1:1)	0.40	0.40

Preparation of trans-Dibenzoylstilbene

Dibenzoylstilbene was isolated by treating the product of the

deoxybenzoin/thionyl chloride reaction with triphenylphosphine<sup>44</sup>. Yield 19%. m.p. 225-6°C (Lit. 230°C). The infrared spectrum was in agreement with literature values<sup>46</sup>. The reaction also gave triphenylphosphine sulphide as a product.

## Preparation of Chlorosulphinyldiphenylmethane

Diphenylmethane (0.1 mole) was treated with thionyl chloride (0.13 mole) and anhydrous aluminium chloride (0.005 mole) under reflux for one hundred and twenty hours. The solution turned dark red after one hour and remained that way for the duration of the reaction. Thionyl chloride was removed under reduced pressure and the dark red liquid was distilled under vacuum through a short column. 1st fraction; b.p. 90-100°C (1.0 mmHg) Yield 32% 2nd fraction; b.p. 110-112°C (1.0 mmHg) Yield 40% The first fraction was unchanged diphenylmethane. The second fraction was slightly yellow but turned black when stored at room temperature for several days. Analysis showed that this material contained sulphur and chlorine.

n.m.r. (CCl<sub>4</sub>): Singlet τ 4.00 1 proton Multiplet τ 2.60-2.90 10 protons i.r. (thin film): 3090(m), 3060(m), 3015(m), 1600(m), 1585(w), 1495(s), 1450(s), 1265(m), 1220(m), 1180(m), 1160(w), 1080(s), 1030(s), 1020(w), 1005(w), 825(m), 750(s), 700(s) cm<sup>-1</sup>.

The residue left in the distillation flask (28%) was a viscous red oil. n.m.r. (CDCl<sub>3</sub>): Multiplet τ 2.60-2.90 i.r. (thin film): 3090(w), 3060(m), 3030(m), 1600(m), 1585(shoulder), 1495(s), 1450(s), 1080(m), 1030(m), 750(s), 700(s) cm<sup>-1</sup>.

Three solutions were compared using thin-layer chromatography on 20 cm. plates spread with silica-gel. The solutions were (a) the

-21-

residual red oil from the diphenylmethane reaction, (b) chlorosulphinyldiphenylmethane and (c) an authentic sample of tetraphenylthiiran (p. 34). The spots were developed by spraying the plates with a solution of iodine in chloroform and the results are set out below.

Solution	Solvent	
	с <sub>6</sub> н <sub>6</sub> ссі <sub>4</sub> (3:1)	cc14
(a)	0.85*	0.47*
(b)	0.80	0.57
(c)	0.85	0.48

# Rf Values

\* A residue was left on the base line.

2.4.4. The Reactions of Thionyl Chloride with a Miscellaneous Group of Compounds

A variety of compounds were treated with thionyl chloride in order to investigate its usefulness in organic synthesis. Where no distinct compound was isolated the reaction products were only partially investigated and no attempt was made to characterise them. The results of the investigation are given in the table overleaf.

Compound	Reaction Conditions	Product
C1CH2C02Et	Reflux, 5 days	No reaction
BrCH2C02Et	Reflux, 5 days	No reaction
PhCH <sub>2</sub> CO <sub>2</sub> Et	Reflux, 5 days	Diphenylmaleic anhydride. Yield 4%.
PhCH <sub>2</sub> CO <sub>2</sub> Me	Reflux, 4 hours	Brown powder. Insoluble in organic solvents. Polymeric.
p-NO2C6H4CH2CO2Et	Reflux, 5 days	No reaction
PhCOCH	Room temperature	Thick oil (+)ve test with
PhCOCH2CH3	Room temperature	Thick oil phenylhydrazine
CH2(CH2)4CO	Room temperature	Brown solid. Polymeric.
CH3COCOCH3	Room temperature	Brown solid. Polymeric.
CH3COCH2COPh	Room temperature	Black oil
сн <sub>3</sub> сосн <sub>2</sub> сосн <sub>3</sub>	Room temperature	Red oil. Mixture of sulphides.
PhCOCH2C02Et	Room temperature	Yellow cil. Evolves H <sub>2</sub> S when dissolved in organic solvents.

2.4.5 The Action of Thionyl Chloride on  $\alpha$ -Alkyl substituted Compounds The Reaction of Thionyl Chloride with 3-Methylpentane-2,4-dione

3-Methylpentane-2,4-dione (5 cm.<sup>3</sup>, p.29) and thionyl chloride  $(3 \text{ cm.}^3)$  were stirred together at room temperature for twenty-four hours. The solution turned red after two minutes and evolved hydrogen chloride. Thionyl chloride was removed under reduced pressure leaving a dark red oil.

n.m.r. (CDCl<sub>3</sub>): In addition to unchanged starting material, there were new singlets at  $\tau$  8.25 and  $\tau$  7.70 in the ratio of 1:2.

The Reaction of Thionyl Chloride with Ethyl 2-cyanopropionate

Ethyl 2-cyanopropionate (0.05 mole, p.30 ) and thionyl chloride

(0.08 mole) were heated together under reflux conditions for fortyeight hours and then distilled under vacuum. 1st fraction 86-90°C (9 mmHg) Yield 85% 2nd fraction 70-72°C (1 mmHg) Yield 12% The first fraction was ethyl 2-cyanopropionate. The n.m.r. spectrum of the second fraction showed that the quartet due to the methine proton of the starting material had disappeared.

n.m.r. (CCl<sub>4</sub>): Triplet  $\tau$  8.65 3 protons Singlet  $\tau$  8.10 3 protons Quartet  $\tau$  5.65 2 protons

The compound decomposed before further analysis was possible. Unfortunately, all attempts at repeating the preparation failed because no reaction between thionyl chloride and the ester could be made to occur again.

The Reaction of Thionyl Chloride with Ethyl a-methylacetoacetate

Ethyl  $\alpha$ -methylacetoacetate (0.05 mole, p.30) was treated with thionyl chloride (0.08 mole) at room temperature for four days. No reaction occurred and so the mixture was heated under reflux for one hour. The solution turned red and evolved hydrogen chloride. Thionyl chloride was removed under reduced pressure. The red oil that remained contained unchanged ester plus a compound giving rise to the following n.m.r. signals.

Triplet	τ 8.60	3 protons
Singlet	τ 8.20	3 protons
Singlet	τ 7.65	3 protons
Quartet	τ 5.65	2 protons

The Reaction of Thionyl Chloride with 3,3-Dimethylpentane-2,4-dione

No reaction occurred when thionyl chloride and 3,3-dimethylpentane-2,4-dione (p.31) were stirred together overnight.

#### 2.4.6 The Action of Thionyl Chloride on Proposed Intermediates

A number of proposed reaction intermediates were treated with thionyl chloride. In this section, each different compound treated in this way is given a new heading.

#### Tetraethoxycarbonylethane

Tetraethoxycarbonylethane (0.05 mole, p.39) and thionyl chloride (0.10 mole) were refluxed together for six hours. No reaction occurred. Ethyl  $\alpha$ -chloroacetoacetate

Ethyl  $\alpha$ -chloroacetoacetate (0.05 mole) and thionyl chloride (0.10 mole) were stirred together at room temperature for sixteen hours. No reaction occurred.

#### Di (acetyle thoxycarbonyl) methyl sulphide

The sulphide (0.05 mole) and thionyl chloride (0.10 mole) were stirred together at room temperature for thirty-six hours. The sulphide dissolved immediately and the solution gradually turned dark green. The thionyl chloride was removed under reduced pressure leaving a dark green semi-solid. An n.m.r. spectrum showing a new singlet at  $\tau$  5.10 and an increase in complexity of the ethyl and methyl signals is indicative of the presence of ethyl  $\alpha$ -chloroacetoacetate.

## Methyl 2-chlorosulphinylpropionate

Methyl 2-chlorosulphinylpropionate (0.05 mole, p.33) and thionyl chloride (0.1 mole) were heated together under reflux for twelve hours. Hydrogen chloride was evolved slowly during this period. After all the excess thionyl chloride had been removed, the yellow oil was passed down a silica-gel column by eluting with chloroform. The major product was a pale yellow oil which solidified on standing. The product contained no sulphur or chlorine.

n.m.r. (CDCl<sub>z</sub>): Singlet 7 7.90

## Singlet $\tau$ 6.10

The integration figure of each peak was identical. The infrared

-25-
spectrum was, in many ways, similar to that of diethyl fumarate and the product was assigned the structure of dimethyl dimethylfumarate. Chlorosulphinyldiphenylmethane

Chlorosulphinyldiphenylmethane was distilled from the reaction mixture of thionyl chloride and diphenylmethane. The sulphinyl chloride (0.025 mole) was treated with thionyl chloride (0.05 mole) under reflux for forty-eight hours. The solution gradually turned red. Excess thionyl chloride was removed under reduced pressure and the red oil was analysed by thin-layer chromatography and n.m.r. spectroscopy. n.m.r. (CDCl<sub>3</sub>): Reaction was incomplete, but n.m.r. showed that most of the sulphinyl chloride had reacted since the singlets at  $\tau$  2.85 and  $\tau$  4.05 had decreased in intensity. A new peak had appeared at  $\tau$  2.95 which corresponded to the singlet of tetraphenylthiiran (p.34). T.l.c. was used to compare the red oil with the samples studied in the diphenylmethane/thionyl chloride reaction (p. 21). The oil contained tetraphenylthiiran and thus it was evident that tetraphenylthiiran is produced when chlorosulphinyldiphenylmethane is treated with thionyl chloride.

### Ethyl 3-ethoxycrotonate

When equimolar proportions of thionyl chloride and ethyl 3-ethoxycrotonate (p.32) were mixed together at room temperature, a vigorous reaction occurred. Hydrogen chloride was liberated and the solution turned from colourless to very dark red in five minutes. No recognisable product could be obtained from the reaction mixture, but the rapidity of the reaction was a useful piece of evidence for the proposed mechanism (Chapter 5).

# 2.5. Reactions of Disulphur Dichloride (S<sub>2</sub>Cl<sub>2</sub>)

Disulphur dichloride was used in preference to sulphur dichloride because of its greater stability. Since reagent grades contain impurities, disulphur dichloride was always distilled over sulphur

-26-

(2% w/v) and charcoal (1% w/v) before use. b.p.  $60-62^{\circ}C$  (50 mmHg). The distillate is then free from the sulphur dichloride and chlorine that occur because of the equilibrium,

2SC1<sub>2</sub> = S<sub>2</sub>C1<sub>2</sub> + C1<sub>2</sub>

# 2.5.1. Preparation of Tetra-substituted Alkenes Preparation of Diethyl dicyanofumarate

The method used was similar to that of Naik<sup>28</sup>. Ethyl cyanoacetate (0.1 mole) and disulphur dichloride (0.2 mole) were stirred together in a round-bottomed flask protected by a calcium chloride drying tube. The flask was immersed in an oil-bath at 100°C for two hours. Hydrogen chloride was evolved for three-quarters of an hour but stirring was continued until the solution blackened. On cooling to room temperature, the solution became a solid mass of crystals with a layer of sulphur at the bottom. The crystals were extracted with boiling petroleum ether  $(80-100^{\circ})$  and recrystallised from the same solvent. White needles. Yield 55%. m.p. 115-6°C (Lit. Naik quoted 117°C but, incorrectly, gave the structure as diethyl dicyanosuccinate.) Nuclear magnetic resonance and infrared spectra were identical to those of the product from the ethyl cyanoacetate/thionyl chloride reaction.

## Preparation of Tetraethoxycarbonylethene

The method of Naik<sup>28</sup> was used. The product was recrystallised from petroleum ether (40-60°). White plates. Yield 40%. m.p.  $50-51^{\circ}C$ (Lit.  $50-51^{\circ}C$ )<sup>28</sup>. The nuclear magnetic resonance spectrum and infrared spectrum were identical to those of the product from the diethyl malonate/thionyl chloride reaction.

### 2.5.2. Reaction with Dimethyl Malonate

Dimethyl malonate (0.05 mole) and disulphur dichloride were heated together at 70°C. When this temperature was reached, a small piece of anhydrous aluminium chloride was added. There was a vigorous evolution of hydrogen chloride, and when this stopped the solution was

-27-

allowed to cool to room temperature. White crystals formed which were filtered off and recrystallised from ethanol. m.p. 175-6°C. Yield 35%. (Found: C,32.2; H,3.3; S,32.8.  $C_{10}H_{12}O_8S_4$  requires C,30.9; H,3.1; S,33.0%).

n.m.r. (CDCl<sub>3</sub>): Singlet τ 6.10 i.r. (KBr disc): 2960(m), 1740(s), 1725(s), 1435(m), 1250(broad), 1045(m), 1025(m), 955(w), 900(w), 840(w), 800(w), 765(w) cm<sup>-1</sup>.

The mass spectrum is given in Figure 3.

2.5.3. Preparation of Sulphides

Preparation of Di(acetylethoxycarbonyl)methyl sulphide

The method used was that of Gompper et al.<sup>43b</sup>. Yield of white crystals, 40%. m.p. 115-116°C (Lit. 83-84°C)<sup>43b</sup>. The literature melting point was probably low because of sulphur impurities. Nuclear magnetic resonance and infrared spectra were identical to those of the solid product from the ethyl acetoacetate/thionyl chloride reaction. Preparation of Bis(1,1-diacetyl)ethyl sulphide

3-Methylpentane-2,4-dione  $(3 \text{ cm}^3)$  and disulphur dichloride  $(1 \text{ cm}^3)$ were stirred together at room temperature in 13 cm<sup>3</sup> of petroleum ether  $(60-80^{\circ})$ . Hydrogen chloride was evolved, and after one hour the solvent was removed under reduced pressure. The residual oil was dissolved in ethanol (15 cm<sup>3</sup>) and cooled to  $-20^{\circ}$ C. White fluffy crystals appeared and were quickly filtered off. m.p. 59-60°C. Yield 38%. (Found: S,10.6.  $C_{12}H_{18}O_4S$  requires 12.4%). n.m.r. (CDCl<sub>3</sub>): Singlet  $\tau$  8.42 6 protons

Singlet 7 7.75 12 protons

i.r. (KBr disc): 2990(w), 2910(w), 1695(s), 1440(w), 1420(m), 1380(m), 1360(s), 1225(m), 1180(s), 1095(m), 1080(m), 1025(m), 970(m), 955(m), 825(w) cm<sup>-1</sup>.

-28-



# 2.6. Reactions of Sulphuryl Chloride (SO2C12)

Sulphuryl chloride was used to synthesise chlorinated compounds. Following Wyman's method<sup>47</sup>, pure products were obtained from the reactions of sulphuryl chloride with (a) diethyl malonate, giving diethyl  $\alpha$ -chloromalonate, and (b) ethyl acetoacetate, giving ethyl  $\alpha$ -chloroacetoacetate and ethyl  $\alpha$ , $\alpha$ -dichloroacetoacetate.

An attempt to prepare chlorodiphenylmethane from diphenylmethane and sulphuryl chloride was unsuccessful.

2.7. Preparation of  $\alpha$ -alkyl substituted compounds

# Preparation of 3-Methylpentane-2, 4-dione

(1) When acetylacetone is alkylated, a mixture of products is obtained because of the non-specific attack of the alkyl carbonium ion on the  $\alpha$ - and  $\gamma$ -carbon atoms. Taylor et al.<sup>48</sup> claim a 100% yield of 3-methylpentane-2,4-dione when acetylacetonatothallium (I) is treated with methyl iodide. This method was used. The product was a colourless liquid. b.p. 80-82°C (25 mmHg). Yield 95% (based on the weight of acetylacetonatothallium (I)).

n.m.r. (CCl<sub>4</sub>): Doublet  $\tau$  8.75<sup>k</sup> Singlet  $\tau$  8.20<sup>e</sup> Singlet  $\tau$  7.95<sup>e</sup> Singlet  $\tau$  7.88<sup>k</sup> Quartet  $\tau$  6.25<sup>k</sup> Singlet  $\tau$ -6.20<sup>e</sup>

'e' denotes that the peak is from the enol tautomer and 'k' that it is from the keto tautomer.

(2) When a further preparation of 3-methylpentane-2,4-dione was necessary it was decided to use the potassium salt of acetylacetone. Although the thallium method was good, it was not practicable to use it on a large scale. The method used was a slight modification of the one devised by Johnson<sup>49</sup>. Acetylacetone (0.3 mole), iodomethane

-29-

(0.32 mole), anhydrous potassium carbonate (45 g) and acetone (75 cm<sup>3</sup>) were stirred in a flask heated in a water-bath at 60°C. After four and a half hours, a 1:1 mixture of petroleum ether (60-80°) and acetone (about 150 cm<sup>3</sup> of solvent) was added to the flask. The reaction mixture was filtered through a sintered-glass filter-funnel and the solid residue was washed three times with more of the solvent mixture. The solvent was removed, under reduced pressure, from the combined filtrates and the remaining liquid was distilled through a short column to give a colourless liquid. b.p. 168-170°C. Yield 90%. The product was identical to that obtained by the thallium route. Preparation of Ethyl  $\alpha$ -methylacetoacetate

Sodium metal (0.2 mole) was dissolved in ethanol (200 cm<sup>3</sup>). When solution was complete, ethyl acetoacetate (0.2 mole) and iodomethane (0.2 mole) were added and the mixture refluxed overnight. The ethanol was removed under reduced pressure, the reaction mixture was filtered and the filtrate was distilled under vacuum. b.p.  $78-9^{\circ}C$  (10 mmHg). Yield 70%.

.m.r. (CC1 <sub>4</sub> ):	Doublet	τ 8.75 <sup>k</sup>
	Singlet	τ 8.70 <sup>e</sup>
	Triplet	$\tau 8.70^{e,k}$
	Singlet	τ 8.00 <sup>e</sup>
	Singlet	τ 7.80 <sup>k</sup>
	Quartet	τ 6.50 <sup>k</sup>
	Quartet	τ 5.80 <sup>e,k</sup>
	Singlet	T=2.70 <sup>e</sup>

n

'e' denotes enol tautomer, 'k' denotes keto tautomer.

### Preparation of Ethyl 2-cyanopropionate

The method of Pollack<sup>50</sup> was used. 2-cyanopropionic acid was esterified using 200 cm<sup>3</sup> of absolute ethanol and 5 cm<sup>3</sup> of concentrated sulphuric acid for each mole of acid. The product was a colourless

-30-

liquid. b.p.  $80-81^{\circ}C$  (10 nmHg). Overall yield 22%. n.m.r. (CCl<sub>4</sub>): Triplet  $\tau 8.70$ Doublet  $\tau 8.45$ Quartet  $\tau 6.30$ Quartet  $\tau 5.70$ 

### Preparation of 3,3-Dimethylpentane-2,4-dione

(1) The sodium salt of 3-methylpentane-2,4-dione was prepared by slowly adding sodium hydride (0.1 mole) to a solution of the dione (0.1 mole) in benzene. Iodomethane did not react with the sodium salt either in a benzene solution or in the absence of a solvent.

(2) The method of Hauser and Adams<sup>51</sup> was modified to use boron trifluoride-etherate instead of the gas. Acetic anhydride (0.3 mole) and isopropyl methyl ketone (0.15 mole) were placed in a round-bottomed flask protected by a calcium chloride drying-tube. Boron trifluorideetherate (0.15 mole) was added and the mixture stirred at room temperature for twenty-four hours. After this time the mixture was poured into a solution of sodium acetate (40 g) in water (300 cm<sup>3</sup>) and then steam-distilled. The distillate was extracted three times with diethyl ether and the solution dried over anhydrous calcium chloride. The ether was removed under reduced pressure and the remaining liquid distilled under vacuum. b.p. 69-71°C (20 mmHg). Yield 29%. n.m.r. (CCl<sub>A</sub>): Singlet  $\tau 8.70$  The integration for

Singlet 7.90 each peak was equal.

### 2.8. Preparation of Esters

#### Preparation of t-Butyl cyanoacetate

Cyanoacetic acid was prepared from chloroacetic acid<sup>52</sup>, and the ester was obtained by treating cyanoacetyl chloride with t-butanol in the presence of  $\underline{N}, \underline{N}$ -dimethylaniline<sup>53</sup>. The cyanoacetate was then distilled under vacuum. b.p. 70-71°C (1 mmHg).

-31-

n.m.r. (CCl<sub>4</sub>): Singlet 78.50 9 protons

Singlet 7 6.55 2 protons

#### Preparation of Methyl phenylacetate

An adaptation of a method due to  $Vogel^{54a}$  was used. The starting materials were phenylacetic acid (0.2 mole), methanol (2.0 mole) and concentrated sulphuric acid (8 cm<sup>3</sup>). The mixture was refluxed for six hours and the final product was a colourless liquid. Yield 76%. b.p. 218-220°C (Lit. 215°C)<sup>54b</sup>.

1.m.r.	(CC1 <sub>4</sub> ):	Singlet	τ 6.50	2	protons
		Singlet	τ 6.46	3	protons
		Singlet	τ 2.75	5	protons

#### Preparation of Methyl propionate

An adaptation of a method due to Vogel<sup>54c</sup> was used. Propionic anhydride (100 cm<sup>3</sup>), methanol (100 cm<sup>3</sup>) and anhydrous zinc chloride (0.3 g) were refluxed together for two hours. The methanol was distilled off and the fraction boiling between 66° and 90°C was collected. This was washed with water and potassium carbonate solution, and dried over anhydrous potassium carbonate. The colourless liquid was redistilled through a short column and the main fraction collected. Yield 30%. b.p. 79-80°C (Lit. 79°C)<sup>54d</sup>.

n.m.r. (CC1 <sub>4</sub> ):	Triplet	τ	8.90	3	protons	
		Quartet	τ	7.70	2	protons
		Singlet	τ	6.35	3	protons

### Preparation of Ethyl 3-ethoxycrotonate

The first part of the synthesis required the preparation of ethyl 3-chlorocrotonate in a two-stage process using the methods of D.E. Jones et al<sup>26</sup>, and Scheibler and Voss<sup>55</sup>. Ethyl 3-ethoxycrotonate was then prepared by treating the chlorocrotonate with sodium ethoxide<sup>26</sup>. The product was distilled under vacuum and gave a white solid, m.p. 30-31°C. Yield 55%.

n.m.r.	(CDC13):	Triplet	T	8.75	3	protons
		Triplet	τ	8.65	3	protons
		Singlet	τ	7.70	3	protons
		Quartet	τ	6.15	2	protons
		Quartet	τ	5.80	2	protons
		Singlet	τ	4.85	1	proton

#### 2.9. Preparation of Sulphinyl Chlorides

## Preparation of Methyl 2-chlorosulphinylpropionate

The general procedure of Douglass and Farah was adopted  $^{56}$ . It is important that the correct stoichiometric quantities are used to obtain optimum yield. Methyl 2-mercaptopropionate (0.25 mole) and glacial acetic acid (0.25 mole) were stirred together in a round-bottomed flask. Chlorine (0.5 mole) was condensed in a flask cooled to  $-70^{\circ}$ C. It was then allowed to bubble through the reaction mixture at a rate controlled by the latent heat of vaporisation of the liquid chlorine. After one hour all the chlorine had been absorbed, and the reaction mixture was warmed to  $35^{\circ}$ C and maintained at that temperature for another hour to expel hydrogen chloride gas. The pale yellow liquid was distilled under vacuum. Yield 85%. b.p.  $54-55^{\circ}$  (1 mmHg).

n.m.r. (CCl<sub>4</sub>): Doublet 7 8.35 3 protons

Singlet 7 6.20 3 protons

Quartet  $\tau$  5.65 1 proton

i.r. (thin film): 3000(w), 2860(m), 2800(w), 1740(s), 1450(s), 1440(s), 1380(s), 1310(s), 1220(s), 1150(s),

1105(m), 1065(s), 1050(m), 955(m), 860(s),

765(m) cm<sup>-1</sup>.

Preparation of 9-Chlorosulphinylfluorene

(a) Preparation of 9-lithiofluorene

Sodium-dried diethyl ether  $(50 \text{ cm}^3)$  and freshly cut lithium (2.2 g) were placed in a three-necked flask. An atmosphere of nitrogen

was maintained throughout the experiment. n-Butyl bromide (17.25 g in  $25 \text{ cm}^3$  of ether) was slowly added to the lithium in ether while the mixture was stirred vigorously. The reaction started almost immediately. While n-butyl bromide was being added the temperature was kept at  $-10^{\circ}$ C, but was allowed to warm to  $10^{\circ}$ C after half an hour and stirring was continued for a further hour. The ethereal solution of n-butyl-lithium was filtered quickly through a wad of glass wool to remove unchanged lithium. Fluorene (0.1 mole, 2 g at a time) was added to the filtrate, and the solution turned red and evolved butane. The solution was heated under reflux for one hour.

(b) Preparation of 9-chlorosulphinylfluorene

Ether was added to the red solution of 9-lithiofluorene to make it up to 400 cm<sup>3</sup>. Sulphur dioxide was bubbled through the well-stirred solution at -60°C. A yellow precipitate formed but disappeared as more sulphur dioxide was bubbled into the solution. Thionyl chloride (0.1 mole) was added to the final colourless solution and the temperature allowed to rise to 20°C. A yellow precipitate of lithium chloride formed and was filtered off. A brown semi-crystalline solid remained when the ether was removed under reduced pressure.

i.r. (thin film): 3060(s), 3040(s), 3020(s), 2950(s), 2920(s), 1910(w), 1810(w), 1715(m), 1610(m), 1480(m), 1450(s), 1400(m),

1300(m), 1190(s), 1150(s), 955(m), 780(m), 730(s) cm<sup>-1</sup>.

2.10. Preparation of Thiirans

# Preparation of 2,3-Epithio-1,2,3,4-tetraphenylbutane-1,4-dione

The method of Kresze and Wucherpfennig<sup>57</sup> was used in which deoxybenzoin was treated with <u>N</u>-sulphinyl-p-toluenesulphonamide in the presence of anhydrous aluminium chloride. The product was identical to that obtained from the reaction of deoxybenzoin with thionyl chloride. Preparation of Tetraphenylthiiran

-34-

### (a) Preparation of benzophenonehydrazone

Benzophenone (40 g) in absolute ethanol (150 cm<sup>3</sup>) was treated with 100% hydrazine (41.2 g), refluxed for ten hours and then cooled in ice. White crystals formed which were filtered off and washed with cold ethanol. m.p.  $95^{\circ}$ C (Lit.  $97-98^{\circ}$ C)<sup>58</sup>. Yield 91%.

(b) Preparation of tetraphenylthiiran

The procedure of J.B. Miller<sup>59</sup> was used to prepare diphenyldiazomethane from benzophenonehydrazone. The diazomethane was then treated with sulphur<sup>60</sup> to give tetraphenylthiiran. The reaction did not proceed as quickly as expected but the red colour of diphenyldiazomethane had disappeared after forty-eight hours. The product was a white crystalline solid, m.p.  $170-1^{\circ}C$  (Lit.  $178^{\circ}C$ )<sup>60</sup>.

n.m.r. (CDCl<sub>z</sub>): Singlet T 2.95

i.r. (KBr disc): 3080(m), 3050(m), 3010(m), 1600(m), 1580(shoulder), 1490(s), 1445(s), 1080(m), 1030(m), 1000(m), 790(s), 755(s), 700(s) cm<sup>-1</sup>.

Attempted preparation of Diethyl 2,3-dicyanothiiran-2,3-dicarboxylate

(a) Preparation of diethyl 2,3-dicyano-oxiran-2,3-dicarboxylate

The epoxide was prepared using Linn's method<sup>61</sup> and was recrystallised from a mixture of diethyl ether and petroleum ether  $(30-40^{\circ})$ . m.p.  $61-69^{\circ}C$  (Lit.  $61-70^{\circ}C$ )<sup>61</sup>.

(b) Treatment of the epoxide with thiourea.

Bordwell and Anderson<sup>62</sup> have successfully used thiourea to prepare thiirans from epoxides and a modification of their procedure was used. The epoxide (6.2 g) was gradually added to a stirred solution of thiourea (2.5 g) in water (15 cm<sup>3</sup>) and concentrated sulphuric acid (0.85 cm<sup>3</sup>). The epoxide dissolved within half an hour and a brown salt began to precipitate which was filtered off after twenty hours. Yield 30%.

The salt was added to four times its own weight of water and made

alkaline (pH 9) with sodium carbonate solution (10% w/v). The result was a black tar. In a second attempt, the aqueous suspension of the salt was maintained at  $0^{\circ}$ C while the alkaline solution was slowly added. There was some effervescence after which the solution was extracted with diethyl ether. Evaporation of the ether left a red oil that was almost insoluble in most organic solvents. Yield approximately 1%.

(c) Treatment of the epoxide with potassium thiocyanate

Hydrothiocyanic acid (HSCN) was prepared<sup>63</sup> and added (in excess) to a suspension of the epoxide in dry diethyl ether. The epoxide dissolved immediately and a precipitate started to form after fifteen minutes. The precipitate was filtered off after twelve hours but subsequent treatment with methanolic potassium hydroxide solution failed to give any usable product.

#### 2.11. Preparation of Thiols and Disulphides

#### Preparation of Methyl 2-mercaptopropionate

The procedure of Eugster and Allner<sup>64</sup> was used to prepare the ester in a two-stage synthesis. 2-Bromopropionic acid was converted to 2-mercaptopropionic acid using sodium disulphide followed by reduction with zinc and hydrochloric acid. The acid was esterified with methanol and the end product was distilled to give a colourless liquid with a very strong and penetrating odour.

n.m.r.	(cc1 <sub>4</sub> ):	Doublet	τ 8.50	21	5 protons
		Doublet	τ 7.70	1	proton
		Quintet	τ 6.42	1	proton
		Singlet	τ 6.28	27	protons

#### Attempted preparation of Di(diethoxycarbonyl)methyl disulphide

(1) Diethyl bromomalonate was prepared by adding bromine to diethyl malonate in carbon tetrachloride<sup>65</sup>. It was then used to prepare a sodium alkylthiosulphate (Bunte's salt)<sup>66</sup>. Diethyl bromomalonate (0.1 mole), sodium thiosulphate (0.1 mole), water (50 cm<sup>3</sup>) and ethanol

-36-

 $(50 \text{ cm}^3)$  were heated together under reflux for eighteen hours. The solution immediately turned yellow but the colour slowly disappeared during the course of the reaction. The mixture was allowed to cool to room temperature, 30% hydrogen peroxide  $(13 \text{ cm}^3)$  was added and the resulting solution was left to stand for twenty-four hours. This solution was extracted with diethyl ether and the ethereal extracts were dried over anhydrous magnesium sulphate. A yellow oil remained after the ether had been removed under reduced pressure. Although two qualitative tests for disulphides<sup>67</sup> were positive, n.m.r. and g.l.c. indicated that the yellow oil was composed of over 95% diethyl malonate.

(2) An attempt was made to follow the procedure of Wolff and Ott<sup>68</sup> but, even after several tries, their experimental results were not reproduced. A mixture of diethyl malonate and disulphur dichloride was heated to 65-70°C and a piece of anhydrous aluminium chloride added. A vigorous evolution of hydrogen chloride occurred for several minutes. The mixture was stirred for one hour. It is claimed that a semi-crystalline oil results on cooling but this did not happen. The reaction was tried at room temperature in case the disulphide was being decomposed by heat. The product was, in all cases, a yellow oil and results indicated that tetraethoxycarbonylethene was the major product but a definite characterisation was not attempted.

## Attempted preparation of Diethyl mercaptomalonate

An adaptation of the method of Baker et al<sup>69</sup> was used. Diethyl bromomalonate was slowly added to an ethanolic potassium hydrosulphide solution,

(a) followed by heating under reflux for thirty minutes,

(b) while keeping the temperature of the solution at 0°C. In the first case the solution turned brown and a yellow precipitate formed. When neutralised with glacial acetic acid the solution became colourless. It was filtered to remove the yellow precipitate and

-37-

extracted with benzene. The product was a colourless liquid, diethyl malonate, and the precipitate was sulphur. Using the conditions in (b), the result was exactly the same. There was a strong, repugnant odour indicating that the thiol may have been formed, but was present in very small amounts by the end of the experiment.

### 2.12. Preparation of Other Compounds

## Preparation of Triethyl 1.2.3-tricyanocyclopropane-1.2.3-tricarboxylate

The sodium salt of ethyl cyanoacetate was prepared by adding the ester (warmed to  $60^{\circ}$ C) to a boiling solution of sodium ethoxide in ethanol, and allowing the mixture to cool. The sodium salt crystallised out of solution, was filtered off and washed with diethyl ether.

To 13 g of the sodium salt suspended in diethyl ether, was added 25 g of iodine in diethyl ether  $(150 \text{ cm}^3)$ . The ether was maintained at reflux temperature for two hours while the iodine solution was added dropwise. The ethereal solution was then washed with sodium thiosulphate solution, to remove the excess iodine, and dried over anhydrous magnesium sulphate. The ether was removed under reduced pressure to leave a red oil which crystallised out to give white crystals. m.p.  $119-20^{\circ}C$  (Lit.  $119^{\circ}C$ )<sup>70</sup>.

# Preparation of 3,4,5,6-tetrachloro-1,2-benzoquinone

The method of Jackson and MacLaurin<sup>71</sup> was used to give the desired product, a red powder, m.p. 131-2°C (Lit. 133°C)<sup>71</sup>.

# Preparation of Ethyl bromocyanoacetate

(A) The same method as that used for the preparation of diethyl bromomalonate<sup>65</sup> was tried but the reaction did not go smoothly. The bromine did not react as it was added to the solution of ethyl cyano-acetate in carbon tetrachloride. After refluxing the mixture, the only product obtained was a yellow infusible solid.

(B) Errara and Perciabosco<sup>70</sup> reported that the desired product could be obtained by brominating ethyl cyanoacetate with bromine-water.

-38-

Stoichiometric amounts of ester and bromine-water were shaken together until the solution was colourless. An oil settled out from the aqueous phase and was removed. After washing with sodium bicarbonate solution the oil was distilled under vacuum. It proved impossible to obtain a pure sample of the mono-bromo ester without using elaborate fractionation equipment. It was decided not to carry the purification any further since diethyl bromomalonate could be used equally well in the place of ethyl bromocyanoacetate and its preparation was much simpler.

#### Preparation of Tetraethoxycarbonylethane

Tetraethoxycarbonylethane was prepared by treating the sodium salt of diethyl malonate with iodine<sup>72</sup>. The product was recrystallised from petroleum ether (40-60°). White crystals, m.p.  $73-74^{\circ}$ C (Lit.  $73^{\circ}$ C)<sup>72</sup>. 2.13. Attempted preparation of Di(acetylethoxycarbonyl)methyl

### sulphoxide

It was thought that di(acetylethoxycarbonyl)methyl sulphoxide was formed as an intermediate in the reaction between ethyl acetoacetate and thionyl chloride. Several attempts were made to oxidise di(acetylethoxycarbonyl)methyl sulphide to the sulphoxide but none was successful. The experiments are listed below under the heading of the oxidising agent used.

(1) Hydrogen Peroxide in Acetone

The reaction of hydrogen peroxide with the sulphide was tried under a variety of conditions between  $0^{\circ}C$  and  $50^{\circ}C$ . The product was either unchanged sulphide or a black oil. The reaction could not be stopped at a stage where all the sulphide had been oxidised to sulphoxide.

(2) Hydrogen Peroxide with a Vanadium Pentoxide catalyst

A solution of hydrogen peroxide in t-butanol was prepared. The procedure of Hardy et al $^{73}$  was followed and although the solution

-39-

turned from yellow to green (indicating some form of oxidation), only unchanged sulphide was recovered.

(3) Manganese Dioxide

A fresh sample of manganese dioxide was prepared<sup>74</sup> and shaken with the sulphide in petroleum ether (40-60°) for ninety-six hours<sup>75</sup>. The solvent was then removed under reduced pressure and the black powder extracted with chloroform in a Soxhlet apparatus. Removal of the chloroform left a red oil that would not crystallise. An infra-red spectrum of the oil showed a peak at 1075 cm<sup>-1</sup>, characteristic of a sulphoxide, but the product could not be isolated pure enough or in sufficient yield to be of any use.

(4) <u>N-Bromosuccinimide</u>

Oxidation of sulphides to sulphoxides has been accomplished using N-bromosuccinimide in methanol<sup>76</sup>. Equimolar proportions of the sulphide and N-bromosuccinimide were added to dry methanol (excess), but some of the solid remained undissolved. The mixture was stirred at room temperature for twenty-four hours and then the methanol was removed under reduced pressure. The product was a brown solid which was dissolved in methylene dichloride and washed with water. Removal of the methylene dichloride gave a mixture of the two starting materials.

The experiment was repeated using t-butanol as the solvent and the temperature was maintained at 50°C. Once again the unchanged starting materials were recovered.

(5) Iodobenzene dichloride

Iodobenzene dichloride was prepared<sup>77</sup> and added to a stirred solution of the sulphide in pyridine as described by Barbieri et al<sup>78</sup>. No reaction occurred, even after twenty-four hours at room temperature.

(6) Sodium Metaperiodate

Leonard and Johnson<sup>79</sup> have used sodium metaperiodate, in water or aqueous methanol, to oxidise sulphides. In this case, however, it was

-40-

found that the sulphide was insufficiently soluble in aqueous methanol to be of any use. A method was tried in which an aqueous solution of sodium metaperiodate was slowly added to a refluxing solution of the sulphide in methanol. The sulphide was unchanged at the end of the reaction but the metaperiodate had been consumed, probably in oxidising the methanol.

An alternative procedure is that of Russell and Ochrymowyez<sup>80</sup> who used sodium metaperiodate in aqueous acetonitrile. All attempts to find the right conditions were unsuccessful. Below 10<sup>o</sup>C, no reaction occurred and above this temperature only a red intractable oil was obtained.

#### Chapter 3

#### MECHANISTIC EXPERIMENTAL PROCEDURES

#### 3.1. Introduction

The experiments included in this chapter were designed to investigate particular aspects of the proposed reaction mechanism or mechanisms. These reactions have already been fully studied with regard to the type of reaction products and have been listed in detail in Chapter 2.

#### 3.2. Gas Evolution Studies

#### 3.2.1. Experimental Details of the Sulphur Dioxide Evolution Study

The apparatus is shown in Figure 4. Two equivalent sets of apparatus were used in parallel, one being used as a 'blank' and the other containing the reaction mixture being studied. The blank gave an estimate of the amount of thionyl chloride carried through the apparatus, since hydrolysis of thionyl chloride to give sulphur dioxide and hydrogen chloride would give an erroneous titration result in the final analysis. The flow of nitrogen through each apparatus was dried, and controlled visually, by bubbling the gas through concentrated sulphuric acid to give, as near as possible, equal flow rates. The reaction vessels were both 50 cm<sup>3</sup> three-necked flasks. The iodine solution was protected from acid spray by glass wool packed loosely in the top of each condenser, and a trap immersed in an ice-salt freezing mixture. The reaction vessels were immersed in an oil bath maintained at  $62^{\circ} \pm 0.5^{\circ}$ C.

Each run was started by adding a measured amount of thionyl chloride to the reaction vessel and flushing out the apparatus with nitrogen. After five minutes the other starting material was injected into the appropriate flask from a syringe, through a rubber septum-cap. In each case the flask already contained six anti-bumping granules, 10 mg of anhydrous aluminium chloride and any other additive needed

-42-



Fig. 4. Gas Evolution Apparatus

for that particular experiment. Each system was then connected to the gas absorption flasks and the rate of flow of nitrogen equalised. The absorption flasks had a volume of about 600 cm<sup>3</sup> and were each fitted with a glass sinter-plate attached to a piece of glass tubing. The gases were led in through the tubing and dispersed into fine bubbles by the glass sinter, thus ensuring an efficient absorption of water soluble gases. The gases from each apparatus were absorbed in equal volumes of standardised iodine solution. Each reading was obtained by removing exactly 10 cm<sup>3</sup> of iodine solution and titrating it against a standardised sodium thiosulphate solution with a 10% (w/v) aqueous solution of starch/urea as the indicator. The results were calculated using a Digico Micro 16 computer (see Appendix I). All the titration solutions were made-up and standardised using the procedures described in Belcher and Nutten<sup>89</sup>.

# 3.2.2. Experimental Details of the Hydrogen Chloride Evolution Study

Essentially the same apparatus and techniques as in Section 3.2.1. were used except for the analysis of the evolved gas. In this case distilled water was used instead of iodine solution, and a silver nitrate titration was required for the chloride ion determination. There are several methods available for determining chloride ion concentration but they all need fairly standardised conditions. This was not easy to ensure since the hydrogen ion concentration continues to rise throughout the reaction and sulphur dioxide is present in ever increasing quantities.

Mohr's method depends on the precipitation of silver chloride before silver chromate in a solution containing the unknown chloride and using potassium chromate as the indicator. The optimum conditions for the titration occur when the solution has a pH of 5.5-10.0; below a pH of 3.8 no end-point is observable. This method and the adsorption indicator method, which is a difficult technique to use accurately, were

-43-

dismissed in preference to Volhard's method. Here the titration is carried out by adding a known excess of silver nitrate to the solution containing chloride ions. Silver chloride is precipitated and the silver ions remaining in solution are titrated against potassium thiocyanate solution with ferric alum as the indicator. At the endpoint a red colouration is observed owing to the formation of a ferrithiocyanate complex. Nitrobenzene is usually added to the solution to coagulate the silver chloride precipitate and prevent adsorption of the thiocyanate ions on to its surface which delays the end-point. The titration is carried out in an acid medium but the need for precise buffering, as in Mohr's method, is not necessary. The titration is not affected by sulphate ions to any great extent but is fairly sensitive to sulphite ions. Since sulphur dioxide is produced in the reaction being studied it was necessary to oxidise the sulphite to sulphate. This was accomplished by adding a dilute solution of potassium permanganate to the titration flasks until the pink colour just remained.

The general procedure used for the analysis was as follows. The solution  $(5.0 \text{ cm}^3)$  to be analysed was pipetted into a flask and potassium permanganate solution added until the pink colour of the permanganate just remained. Standardised silver nitrate solution  $(5.0 \text{ cm}^3)$  and water  $(10 \text{ cm}^3)$  were added, followed by nitrobenzene  $(2 \text{ cm}^3)$ . The solution was shaken and then  $1 \text{ cm}^3$  of the indicator, a saturated solution of ferric alum, was added. Potassium thiocyanate was carefully added from a burette until the red end-point was reached. The results were calculated on a Digico Micro 16 computer (see Appendix II). Titrations were not continued after three hours since the amount of sulphur dioxide present would affect the accuracy of the method.

-44-

#### 3.2.3. Results

#### Sulphur Dioxide

All the results below are reproduceable within the limits of experimental accuracy. The weight of gas evolved was calculated from the titration figures after a correction had been made for each 'blank' reading. The proposed overall equation is.

$$2 \times CH_2 + 2SOCl_2 \longrightarrow > C=C + 4HCl + SO_2 + S$$

For each mole of active methylene compound, half a mole of sulphur dioxide is produced. The sulphur dioxide dissolves in the iodine solution and is oxidised to sulphate.

$$SO_2 + H_2O \longrightarrow 2H^+ + SO_3^-$$
  
 $SO_3^- + I_2 + H_2O \longrightarrow SO_4^- + 2I^- + 2H^-$ 

If the resulting solution is titrated against sodium thiosulphate solution, a direct relationship between the volume of thiosulphate used and the weight of sulphur dioxide evolved, can be derived.

The straightforward reaction between ethyl cyanoacetate and thionyl chloride was studied, and the conditions are given below together with details of the additives designed to affect any possible free-radical reaction.

(1) Reaction; ethyl cyanoacetate (5.0 cm<sup>3</sup>) and thionyl chloride

 $(4.0 \text{ cm}^3).$ 

Blank ; thionyl chloride.

(2) Reaction; ethyl cyanoacetate (5.0 cm<sup>3</sup>), thionyl chloride (4.0 cm<sup>3</sup>) and tetrachloro-p-benzoquinone (5%, w/v).

Reaction; ethyl cyanoacetate (5.0 cm<sup>3</sup>), thionyl chloride (4.0 cm<sup>3</sup>) and dibenzoyl peroxide (0.1%, w/v).

Blank ; ethyl cyanoacetate  $(5.0 \text{ cm}^3)$  and thionyl chloride  $(4.0 \text{ cm}^3)$ .

The results were plotted in the form, weight of sulphur dioxide evolved

-45-

against time. In one case the effect of adding tetrachloro-p-benzoquinone is shown (Fig. 5), and in another case the effect of dibenzoyl peroxide is shown (Fig. 6).

The stoichiometric equation indicates that one mole of sulphur dioxide is evolved for each mole of alkene produced. Analysis of the reaction mixture after each run showed that the yields of alkene and sulphur dioxide differed by an average of 5%. This was a reasonable indication that the errors due to sulphur dioxide dissolving in the reaction mixture, rather than being evolved, were quite small. <u>Hydrogen Chloride</u>

Reaction; ethyl cyanoacetate  $(5.0 \text{ cm}^3)$  and thionyl chloride  $(4.0 \text{ cm}^3)$ .

Blank ; thionyl chloride.

The results were calculated directly from the volume of potassium thiocyanate used for each titration.

Thionyl chloride is evolved in two separate steps of the reaction, during the production of a sulphinyl chloride and also when a sulphine is formed (see Chapter 5). This causes complications when interpreting the results but a full discussion will be found in Section 5.3., and so it is only necessary to indicate here that the amount of hydnogen chloride (x) evolved was converted into the amount of ethyl cyanoacetate that remained (a-x), where (a) was the initial amount of ester present. The best straight lines were obtained by plotting  $1/(a-x)^{\frac{1}{2}}$  against time (Figure 7) and 1/(a-x) against time (Figure 8).

3.3. The Reaction between Diethyl malonate and a mixture of Disulphur dichloride and Sulphuryl chloride

Disulphur dichloride and sulphuryl chloride were freshly distilled and mixed together in equimolar proportions. Diethyl malonate was dried over anhydrous magnesium sulphate and distilled under reduced pressure. The ester was stirred in a flask suspended in an oil-bath

-46-



Fig. 5 Plot of (weight of sulphur dioxide) against time (see p. 46).



Fig. 6 Plot of (weight of sulphur dioxide) against time (see p. 46).

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maintained at  $75^{\circ}$ C. The mixture of disulphur dichloride and sulphuryl chloride was added in a dropwise fashion, and the reaction mixture stirred for four hours. Hydrogen chloride was evolved for the first half hour of the reaction and the solution turned yellow. A qualitative estimate of the reaction products was obtained using gasliquid chromatography and the results are shown in Table 2. <u>Table 2</u> Products obtained from the reaction of Diethyl malonate (0.1 mole) with a mixture of Disulphur dichloride and Sulphuryl chloride.

Reaction Products	S2Cl <sub>2</sub> (0.1 mole) S02Cl <sub>2</sub> (0.1 mole)	S <sub>2</sub> Cl <sub>2</sub> (0.05 mole) SO <sub>2</sub> Cl <sub>2</sub> (0.05 mole)
Diethyl malonate	-	+
Diethyl $\alpha$ -chloromalonate	+	+
Diethyl $\alpha$ , $\alpha$ -dichloromalonate	+	+ (less than
Tetraethoxycarbonylethene	+	+ 5%)

indicates the compound was present at the end of the reaction.
indicates the compound could not be detected at the end of the reaction.

When only 0.05 mole quantities of disulphur dichloride and sulphuryl chloride were used, the reaction was incomplete but there was still a large amount of diethyl  $\alpha$ -chloromalonate present. Thus, it was shown that thionyl chloride did not behave like a mixture of sulphuryl chloride and disulphur dichloride, since no chlorinated product was obtained from the reaction between diethyl malonate and thionyl chloride (p. 15).

# 3.4. The Attempted 'Trapping' of a Carbanion Intermediate

The reagents used to trap the postulated carbanions were compounds containing a labile halogen atom which could be lost, as an anion, to leave a carbonium ion usually stabilised by some form of charge

-47-

delocalisation. The procedure was to treat diethyl malonate with thionyl chloride in the usual way (p. 15), except that the halide was added to the reaction mixture. If a carbanion was formed as an intermediate during the production of a sulphinyl chloride, it was possible that a competetive reaction would occur between the chlorosulphinyl cation and the stable carbonium ion, i.e.

>CH<sub>2</sub> + SOC1<sub>2</sub> ---- > >CH<sup>-</sup> + HC1 + SOC1<sup>+</sup>

Then,  $>CH^- + SOC1^+ \longrightarrow >CHSOC1$ 

or,  $>CH^- + R^+ \longrightarrow >CHR$ 

As well as the expected tetraethoxycarbonylethene, an  $\alpha$ -substituted malonic ester should also be obtained. Details of the trapping experiments are listed below under the headings of each reagent.

(a) Methyl Iodide

Diethyl malonate (0.1 mole), thionyl chloride (0.1 mole) and methyl iodide (0.05 mole) were heated together under reflux conditions for four hours and then distilled under vacuum. All the methyl iodide and 50% of the diethyl malonate was recovered. The residue in the flask was tetraethoxycarbonylethene. The presence of any diethyl  $\alpha$ -methylmalonate should have been easily detected in an n.m.r. spectrum. As well as the usual methylene singlet from the excess diethyl malonate there would be a new doublet and a new quartet from the methyl and methine protons respectively. No diethyl  $\alpha$ -methylmalonate was observed.

(b) t-Butyl Chloride

It was hoped that a t-butyl group rather than a methyl group in the  $\alpha$ -position of the ester would be more easily detectable because of the singlet of nine protons in the n.m.r. spectrum.

The experimental conditions were the same as in (a) above, but t-butyl chloride was used instead of methyl iodide. The alkene was

-48-

once again formed but an n.m.r. spectrum of the volatile components of the reaction mixture was complex. A number of peaks appeared in the region  $\tau$  8.0-9.5 indicating that the t-butyl chloride had undergone decomposition and rearrangement to other alkyl chlorides.

(c) Benzyl Bromide

Benzyl bromide forms a more stable carbonium ion than that obtained from either methyl iodide or t-butyl chloride. It was used in the hope that the carbonium ion would be readily formed in solution and hence react with any carbanion present. The experiment was tried using diethyl malonate, ethyl cyanoacetate, and malononitrile.

(1) Diethyl malonate. No diethyl  $\alpha$ -benzylmalonate was detected when the reactants (0.05 mole quantities) were treated as follows:

(i) Under reflux for four hours or,

(ii) By slow addition of thionyl chloride to the rest of the mixture maintained at 85°C and then stirred at that temperature for three days or,

(iii) As in (ii) except that stirring was only continued for half an hour after the addition of the last of the thionyl chloride.

(2) Ethyl cyanoacetate. Using 0.05 mole quantities and heating under reflux for three hours yielded no ethyl  $\alpha$ -benzyl- $\alpha$ -cyanoacetate.

(3) Malononitrile. Heating the reagents (0.05 mole quantities) under reflux for twenty minutes caused a violent reaction and the apparatus became coated with a black coke-like material. The experiment was repeated without heating but the distillate from the black residue contained no 2-phenylethane-1,1-dicarbonitrile.

(d) Triphenylmethyl Bromide

Diethyl malonate (0.05 mole), thionyl chloride (0.05 mole) and triphenylmethyl bromide (0.025 mole) were heated together under reflux for four hours and then allowed to cool to room temperature. Crystals formed on standing but were not removed. The mixture of crystals and

-49-

solution was dissolved in a minimum volume of petroleum ether  $(60-80^{\circ})$ and fractional crystallisation yielded several batches of crystals consisting of triphenylmethyl bromide and tetraethoxycarbonylethene. The mother liquor contained diethyl malonate but no diethyl  $\alpha$ -triphenylmethylmalonate was detected.

#### 3.5. The Attempted 'Trapping' of a Sulphine Intermediate

An attempt was made to trap the sulphines that are proposed as intermediates in the reaction mechanism (Chapter 5). Sulphines have been trapped before using the ready addition across the carbon-sulphur double bond <sup>90</sup>.



Many compounds react with sulphines and it was decided to attempt to prepare the adduct with 3,4,5,6-tetrachloro-1,2-benzoquinone since the product would probably be a crystalline solid easily separable from the reaction mixture.

Diethyl malonate (0.05 mole) and thionyl chloride (0.05 mole) were heated together under reflux. After five minutes the benzoquinone (0.1 g) was added and within fifteen minutes the bright red colour of the quinone had disappeared. The experiment was repeated using 0.1 mole quantities of all three compounds which were then refluxed for five hours. The red colouration remained and the solution was set aside to crystallise overnight. 1,2-dihydroxy-3,4,5,6-tetrachlorobenzene was isolated in 10% yield. The residue was a red oil which

-50-

was not found to be the required adduct, but merely a mixture of starting materials and tetraethoxycarbonylethene.

The experiment was repeated using ethyl cyanoacetate instead of diethyl malonate, but only a black intractable oil was obtained. <u>3.6. The Attempted Preparation of a 'Cross-product'</u>

If two different active methylene compounds are heated together with thionyl chloride it should be possible to isolate three different alkenes. Two symmetrically substituted alkenes (each in 25% yield) and a 50% yield of an unsymmetrical alkene, formed by the interaction of unlike, but equivalent, reaction intermediates, should in theory be formed. The actual yields will differ due to variations in reaction rates.





(a) Diethyl malonate (0.05 mole) and ethyl cyanoacetate (0.05 mole) were heated under reflux with thionyl chloride (0.3 mole). An n.m.r. spectrum of aliquots drawn from the reaction mixture every half-hour showed that the rates of reaction of the two compounds differed so much that very little triethyl 2-cyanoethene-1,1,2-tricarboxylate was likely to be formed. The ethyl cyanoacetate reacted rapidly whilst the diethyl malonate was not affected.

(b) Experiment (a), above, was repeated with the difference that methyl cyanoacetate was used instead of diethyl malonate. An attempt to separate the crystalline products of the reaction by thin-layer chromatography (t.l.c.) failed. The absorbent was silica-gel spread on 20 cm plates and although a variety of solvents were tried, little

-51-

separation between diethyl and dimethyl dicyanofumarate was achieved. It was not possible to say with any certainty that an intermediate spot corresponding to ethyl methyl dicyanofumarate was present.

(c) Instead of using the ethyl ester, t-butyl cyanoacetate was suggested in the hope that the t-butyl group would cause sufficient differences in the products to allow separation by t.l.c. As mentioned earlier (p.14 ) however, its rate of reaction with thionyl chloride was too rapid to be of any use in this experiment.

# 3.7. The Reaction of Ethyl Cyanoacetate and Thionyl Chloride Studied by N.M.R. Spectrometry

The n.m.r. spectra of two sulphinyl chlorides, chlorosulphinyldiphenylmethane and methyl 2-chlorosulphinylpropionate, show an absorption in the  $\tau$  4-5.5 region. This is attributable to the methine hydrogen on the same carbon atom as the chlorosulphinyl group. It was thought that, in the reaction between ethyl cyanoacetate and thionyl chloride, a sulphinyl chloride would be formed as an intermediate and, hence, a new peak should appear in the n.m.r. spectrum of the reaction mixture. Withdrawing aliquots from the reaction mixture every halfhour, cooling immediately to 0°C and taking an n.m.r. spectrum within five minutes revealed no peak in the region below  $\tau$  5.5.

### 3.8. The Detection of Diethyl Dicyanomaleate

The possible existence of a cis-alkene in the products of the reaction between ethyl cyanoacetate and thionyl chloride was investigated. The reaction was carried out as described earlier (p. 14) except that heating was stopped after two hours. It is well known that cis-isomers are usually more soluble in organic solvents than the corresponding trans form. Diethyl dicyanofumarate is slightly soluble in carbon tetrachloride. The reaction mixture was extracted with carbon tetrachloride (100 cm<sup>3</sup>) at 50°C in the hope that rather more of the cis-isomer than trans-isomer would dissolve. The solvent

-52-

was removed under reduced pressure leaving a yellow semi-solid. The infra-red spectrum showed two new peaks at 2215 cm<sup>-1</sup> (-C=N) and 1630 cm<sup>-1</sup> (C=C). As explained in Chapter 4, these two peaks indicated that a cis-alkene was probably present in the reaction products. Thin-Layer Chromatography (t.l.c.) of the Products

The reaction of ethyl cyanoacetate and thionyl chloride was followed using t.l.c. A sample was withdrawn from the reaction mixture every half-hour and dissolved in chloroform to give a 5% solution (v/v). The t.l.c. plates were spread with silica-gel and the solvent used was a mixture of benzene and chloroform. The spots were developed by spraying the plates with a solution of iodine in chloroform. When a 1:1 mixture of benzene and chloroform was used only two spots were observed, one at  $R_f$  0.30 and the other at  $R_f$  0.15. The former gradually disappeared over the course of the reaction and was attributed to starting material while the latter was found to be the alkene (compared with an authentic sample). The solvent system was changed to a mixture of chloroform and benzene in the ratio 3:1 (v/v). Three spots were then observed with  $R_f$  values of, 0.90 (starting material); 0.44 (probably diethyl dicyanomaleate); 0.23 (diethyl dicyanofumarate).

The only spot that could not definitely be accounted for was that with an R<sub>f</sub> value of 0.44 and so it was assumed to be diethyl dicyanomaleate. Both the lower spots appeared gradually, over the course of the reaction, but the technique did not allow any quantitative estimate to be made of the amount of each isomer present. Preparative t.l.c.

A 20 x 20 cm t.l.c. plate was spread with silica-gel to a thickness of 1.0 mm instead of the usual 0.25 mm. The sample was applied to the plate using a 'streak applicator' to ensure an even distribution. The solvent was run up the plate in the usual way but

-53-

when the run was complete the plate was not sprayed with iodine solution. Two bands of absorbent were scraped off the plate, corresponding to spots at Rf 0.50-0.35 and Rf 0.30-0.15. The sample was eluted from the silica-gel using chloroform which was then evaporated off under reduced pressure until dryness was almost reached. The solutions were analysed by mass spectrometry and found to be almost identical to an authentic sample of diethyl dicyano-

fumarate (Figure 1). There were variations at high molecular weight (>150) which were attributed to impurities from the silica-gel. The similarity between the two mass spectra indicated that the two spots corresponded to the cis- and trans-isomers and were therefore taken to be diethyl dicyanofumarate and diethyl dicyanomaleate.



#### Chapter 4

#### DISCUSSION OF SYNTHETIC EXPERIMENTAL RESULTS

In Chapter 2 no attempt was made to justify the assignation of a particular structure to a compound. In many cases no confirmation was required beyond some form of characterisation, e.g. melting point, boiling point etc., that agreed with the literature value. Where this was not possible, or gave rise to some ambiguity, a further explanation will be found in this chapter.

Thionyl chloride has been shown to give rise to several classes of compounds when treated with compounds containing active methylene groups. The reactions being considered are summarised in Table 3. <u>Table 3.</u> The Reaction Products of SOC1<sub>2</sub> and X-CH<sub>2</sub>-Y

Х - С Н <sub>2</sub> - Ү		Product		
X	Y	Froduct		
-CO2Me	-CN			
-CO2Et	-CN			
-C02Me	-CO2Me			
-CO2Et	-CO2Et	Y Y Y		
-CN	-CN			
Ph	-CN			
-Ph	-Ph	$\frac{Ph}{Ph} \stackrel{S}{\leftarrow} \stackrel{Ph}{\leftarrow} _{Ph} + \frac{Ph}{Ph_2} CHSOC1$		
-Ph	PhCO-	Ph C S COPh PhCO C Ph		
-C0 <sub>2</sub> Me -C0 <sub>2</sub> Et	сн <sub>3</sub> со- сн <sub>3</sub> со-	X-CH-Y X-CH-Y I I S + Cl X-CH-Y		

The reaction between thionyl chloride and ethyl cyanoacetate gave diethyl dicyanofumarate, the first tetra-substituted alkene prepared
in this study. The compound was originally prepared by Naik<sup>28</sup> from the reaction between ethyl cyanoacetate and disulphur dichloride, but he erroneously named it diethyl dicyanosuccinate. Felton<sup>37</sup> prepared the alkene in ten per cent yield using ethyl cyanoacetate and selenium dioxide.

 $2CNCH_2CO_2Et + SeO_2 \longrightarrow C=C CO_2Et + 2H_2O + Se$ EtO\_C CN

He did not seem to be aware of Naik's work and was in doubt about the

structure of the product, as a substituted cyclopropane could well have

been formed.

24.2

i.e.



Preparation of the cyclopropane resolved the problem for him however,

and he assigned the structure of diethyl dicyanofumarate to the oxidation product, although it was some years before Kudo<sup>81</sup> proved its trans-configuration.

When ethyl cyanoacetate was treated with thionyl chloride it was possible that any one of three compounds, the alkene, the succinate or the cyclopropane, had been formed. The n.m.r. spectrum of the product showed only a quartet and a triplet from an ethyl group, which obviously ruled out the succinate alternative. The cyclopropane

structure was still a possibility since neither elemental analysis nor

n.m.r. spectroscopy could distinguish between the two structures.

Preparation of the cyclopropane (p. 38) followed by a mixed melting

point determination resolved the problem, whilst comparison of the

infra-red spectra provided confirmation that the two structures were different.

-56-

The mass spectrum of diethyl dicyanofumarate is shown in Chapter 2, Fig. 1, but an explanation is given below. Table 5 shows the relative intensity of the main peaks and the structure of particular fragments. The mass spectrum of another tetra-substituted alkene, tetramethoxycarbonylethene, is also given (Table 6 and Chapter 2, Fig. 2) so that the two alkenes may be compared and contrasted with the mass spectrum of the unexpected reaction product of dimethyl malonate and disulphur dichloride (Table 7 and Chapter 2, Fig. 3).

Diethyl dicyanofumarate has a weak molecular ion peak (M) at a position corresponding to a molecular weight of 222. Since a molecule with an even-numbered molecular weight contains an even-number of nitrogen atoms it was hence assumed that the compound was diethyl dicyanofumarate.

In Table 4 a list of the percentages of the principal stable heavier isotopes present in some naturally occurring elements is given. Using these figures it is possible to calculate the relative intensity of peaks at M+1 and M+2 compared with the molecular ion peak (M). <u>Table 4</u> Principle Stable Heavier Isotopes<sup>82</sup>

Isotope	Percent of Isotope
13 <sub>C</sub>	1.11
18-	0.015
15 <sub>11</sub>	0.20
33 <sub>S</sub>	0.78
34 <sub>S</sub>	4.4

Diethyl dicyanofumarate has the formula  $C_{10}H_{10}N_2O_4$ . If the intensity of the molecular ion peak is 100 then, using the figures in Table 4 it can be shown that the intensity of the peak at M+1 is 11.9.

-57-

The actual figure was approximately 18, but it could not be measured accurately because of overall low intensity of the peaks at the M and M+1 positions.

In both the tetra-substituted alkenes the strongest peak was given by the ion formed from the parent compound by loss of an alkoxy group. Neither alkene tended to cleave at the carbon-carbon double bond. The fragmentation pattern of tetramethoxycarbonylethene is in many ways similar to that of tetramethyl 1,2,4,5-tetrathian-3,3,6,6-tetracarboxylate because the loss of four sulphur atoms gives an ion that is identical to the molecular ion in tetramethoxycarbonylethene.

# Table 5. Mass Spectrum of Diethyl Dicyanofumarate

Mass-to- Charge Ratio	Relative Intensity	Nature of Fragment (M is the Molecular Ion Peak)					
222	1.7	СN СH <sub>z</sub> CH <sub>2</sub> O <sub>2</sub> C-Ç=C-CO <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> (M)					
207	1.7	M - CH <sub>2</sub>					
194	16	M - C <sub>o</sub> H					
193	15	$M - C_{2}H_{E}$					
178	23	CH <sub>z</sub> CH <sub>2</sub> O <sub>2</sub> C-C=C-CH <sub>2</sub> CH <sub>z</sub>					
177	100	$M - OC_{OH_{E}}$					
176	19	$M = (OC_{OH_{E}} + H)$					
167	21	C_H <sub>E</sub> O_C-C=C-C=O					
166	13.5	$M = 2C_2H_4$					
151	16	C <sub>2</sub> H <sub>c</sub> O <sub>2</sub> C-C=C=CH-CH <sub>z</sub>					
150	63	C <sub>2</sub> H <sub>E</sub> O <sub>2</sub> C-C=C=CH-CH <sub>2</sub>					
149	1.7	$M - CO_2C_2H_5$					
132	16	225 М. 200 <sub>0</sub> H <sub>Б</sub>					
122	40	$M - (CO_2C_2H_5 + HCN)$					
121	5.3	$M = (CO_2C_2H_5 + C_2H_4)$					
106	33.5	0=C-C=C=CH-CH <sub>2</sub>					
105	31	CH <sub>z</sub> CH <sub>2</sub> -C=C-CN					
104	9.7	O=C-C=C-CN					
94	4.7	CN CH <sub>z</sub> -Ç=C-CH <sub>2</sub> CH <sub>z</sub>					
79	13.6	CH <sub>2</sub> CH <sub>2</sub> -C=C-CN					
78	53	CH <sub>3</sub> CH=C=C-CN					
77	95	CH2-CH=C=C-CN or CN-CH-C-CN					
76	37	M - 200 <sub>2</sub> C <sub>2</sub> H <sub>5</sub>					
51	11	CH2-CH=C=C or CH-C-CN					
45	50	oc <sub>2</sub> H <sub>5</sub>					

22

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# Table 6. Mass Spectrum of Tetramethoxycarbonylethene

Mass-to- Charge Ratio	Relative Intensity	Nature of Fragment (M is the Molecular Ion Peak)
260	1.5	(CH <sub>3</sub> 0 <sub>2</sub> C) <sub>2</sub> C=C(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> (M)
256	1.0	М - 4Н
230	10.2	M - 2CH <sub>3</sub>
229	100	M - OCH <sub>3</sub>
198	7.5	M - 20CH3
157	6.9	СН3002С-С=С-С02СН3
140	3.9	CH <sub>3</sub> CO-C(CH <sub>3</sub> )=C(CH <sub>3</sub> )-COCH <sub>3</sub>
111	9.2	CO-C=C-CO <sub>2</sub> CH <sub>3</sub>
99	3.3	CO-C-CO2CH3
83	2.0	CO-C-C-CH3
80	2.0	CO-C=C-CO
67	7.2	со-с=с-сн <sub>3</sub>
64	15.5	CO-C=C-C
59	42	CO <sub>2</sub> CH <sub>3</sub>
53	4.6	С-СНО
45	4.1	CO2H
39	22.5	с-с-снз

Table 7. Mass Spectrum of Tetramethyl 1,2,4,5-tetrathian-3,3,6,6-

tetracarboxylate

Mass-to- Charge Ratio	Relative Intensity	Nature of Fragment (M is the Molecular Ion Peak)
388	4.5	(CH <sub>3</sub> 0 <sub>2</sub> C) <sub>2</sub> C <sup>-S-S</sup> <sub>-S</sub> C(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> (M)
357	1.0	M - OCH3
356	0.8	M - S
329	2.4	$M - CO_2 CH_3$
324	14.2	M - 2S
297	1.7	$M - (S + CO_2 CH_3)$
260	1.6	M - 4S
229	58.5	$M - (4S + OCH_3)$
226	32	(CH <sub>3</sub> 0 <sub>2</sub> C) <sub>2</sub> CS <sub>3</sub>
198	4.3	M - (4S + 20CH <sub>3</sub> )
194	2.4	(CH <sub>3</sub> 0 <sub>2</sub> C) <sub>2</sub> CS <sub>2</sub>
167.	19.5	CH <sub>3</sub> 0 <sub>2</sub> C-CS <sub>3</sub>
162	52	(CH302C)2CS
157	3.6	(CH302C)2C-C-C02CH3
140	2.1	CH <sub>3</sub> O <sub>2</sub> C-C(Me)-C(Me)-CO <sub>2</sub> CH <sub>3</sub>
118	5.8	S-S-COCH2
111	4.4	со-с-с-со <sub>2</sub> сн <sub>3</sub>
. 103	70.5	CH302C-C-S
86	5.0	S-C-COCH2
72	18.6	CO-C-S
64	57	S-S
59	100	со <sub>2</sub> сн <sub>3</sub>
58	23.5	со <sub>2</sub> сн <sub>3</sub>
45	21.5	С-Ѕ-Н
44	14.2	C-S
39	7.5	C-C-CH3

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The infra-red spectra of tetra-substituted alkenes is quite simple but rather uninformative<sup>83</sup>. Symmetry predicts that trans-substituted alkenes do not have an infra-red active carbon-carbon double bond stretching vibration at 1600 cm<sup>-1</sup>. Flett<sup>84</sup>, for example, found no carbon-carbon double bond absorption in fumaric acid. The absence of the usually strong nitrile peak at 2225 cm<sup>-1</sup> may be explained in the same way. It has also been shown that the intensity of a nitrile group absorption is markedly decreased by an adjacent electronwithdrawing group<sup>85</sup>. In the cyano-substituted alkenes that were prepared, a very weak nitrile absorption was discernible in the region 2210-2250 cm<sup>-1</sup>. When an attempt to detect diethyl dicyanomaleate was carried out, the lack of infra-red activity just described was very useful. The cis-alkene has a lower symmetry than the trans and it was possible to observe the presence of a carbon-carbon double bond vibration at 1630 cm<sup>-1</sup> and a nitrile absorption at 2205 cm<sup>-1</sup>.

As shown in Table 3, not all the compounds used gave alkenes on treatment with thionyl chloride. Although the reaction between ethyl acetoacetate and thionyl chloride was known<sup>27</sup>, no spectroscopic data for the resulting sulphide have been recorded. The infra-red spectra of the sulphides from both the ethyl and methyl acetoacetic esters are very similar. There is no indication of a carbon-sulphur single bond absorption, but this is usual since it would appear in the region  $600-700 \text{ cm}^{-1}$  and be too weak to be of any value. The main feature of the spectrum is a broad strong band at  $1600 \text{ cm}^{-1}$ , but virtually no carbonyl absorption at  $1750 \text{ cm}^{-1}$ . This immediately suggests an  $\alpha\beta$ -unsaturated carbonyl group and, together with the broad weak band at  $2700 \text{ cm}^{-1}$ , shows that an enolic structure is present, i.e.



R = Me or Et

-59-

The structure was confirmed by its n.m.r. spectra. The hydrogen atoms on the ester and the methyl groups appeared in their usual positions (pp. 17 and 19) but the remaining two protons had shifted downfield to  $\tau$  - 3.60 in the methyl compound and  $\tau$  - 3.45 in the ethyl compound. This shift can only be accounted for by postulating such an enolic structure.

The other product from the reaction of acetoacetic esters and thionyl chloride, which had not been reported by Michaelis and Phillips<sup>27</sup>, was the alkyl  $\alpha$ -chloroacetoacetate.

 $CH_3 COCHCO_2 R$  R = Me or Et

The ethyl compound was known and so its preparation by a known route 47, from sulphuryl chloride and ethyl acetoacetate, was repeated and the product identified as being the same as that from the thionyl chloride reaction. The very characteristic absorption of the methine proton on the  $\alpha$ -carbon atom att 5.0 in the n.m.r. spectrum enabled the  $\alpha$ -halo derivatives of methyl acetoacetate and diethyl malonate to be readily identified.

As sulphinyl chlorides are important intermediates in the proposed mechanisms it was felt that certain of them should be made and treated with thionyl chloride. Several difficulties were encountered however, the first of which was deciding on which preparative route to use. Probably the best method is by the action of chlorine on thiols or disulphides in acetic acid or acetic anhydride<sup>86</sup>.

 $2RSH + Cl_2 \longrightarrow R-S-S-R + 2HCl$   $R-S-S-R + Cl_2 \longrightarrow 2RSC1 \xrightarrow{2Cl_2} 2RSCl_3$   $RSCl_3 + CH_3CO_2H \longrightarrow RSOC1 + CH_3COC1 + HCl$ 

All attempts at preparing either the disulphide or the thiol of diethyl malonate proved unsuccessful, however, as the compounds were

-60-

unstable under the conditions being used. It is possible that the compounds may be prepared under very carefully controlled conditions but as they were required pure for the next stage of the reaction it is unlikely that they would be stable enough to undergo any form of purification. Hence further steps were not taken to purify the compounds. The instability of these compounds may be attributed to the presence of two strong electron-withdrawing groups on the  $\alpha$ -carbon atom. Another compound was used, therefore, which contained only one electronwithdrawing group and so methyl 2-mercaptopropionate was successfully prepared. Treatment with chlorine in acetic acid gave a good yield of methyl 2-chlorosulphinylpropionate.

It was also decided that 9-chlorosulphinylfluorene would be a useful compound to investigate. The preparation of this sulphinyl chloride is simplified because of the greater ease with which an organo-lithium compound can be prepared from a hydrocarbon compared with an ester. Hence 9-lithiofluorene was treated with sulphur dioxide and then thionyl chloride was added to give 9-cnlorosulphinylfluorene.



It is interesting to note the position of the sulphur-oxygen double bond absorption of sulphinyl chlorides in the infra-red region, since little has been published on the infra-red spectra of these compounds. The three sulphinyl chlorides prepared in this thesis, chlorosulphinyldiphenylmethane, 9-chlorosulphinylfluorene and methyl 2-chlorosulphinylpropionate, correspond well with those obtained in further work on this subject<sup>67</sup>. It appears that the sulphur-oxygen double bond

-61-

in compounds of the general formula R-SO-Cl absorbs in the region  $1150-1200 \text{ cm}^{-1}$ .

The preparation of thiirans caused problems that could not be overcome. The usual method of preparation is the treatment of an epoxide with thiourea or potassium thiocyanate. Preparation of the epoxide derived from tetraethoxycarbonylethene would require a multistage synthesis involving the preparation of pyridine-N-oxide as an intermediate <sup>101</sup>. The epoxide from diethyl dicyanofumarate can be readily made however<sup>61</sup>, and so this was used as the starting material for the preparation of the thiiran. The preparation is a two-stage process<sup>62</sup>.



The intermediate salt was readily formed at room temperature, and was filtered off from the reaction mixture. Attempts to neutralise the salt however gave either a black tarry solution or, if neutralised at  $0^{\circ}$ C, a very small yield of a red oil. A similar result was obtained when an alternative method was used in which potassium thiocyanate was substituted for thiourea.

Although the preparation of thiirans by the normal route was unsuccessful, two thiirans were prepared directly from thionyl chloride reactions. Thus deoxybenzoin and diphenylmethane gave 2,3-dibenzoyl-2,3-diphenylthiiran and tetraphenylthiiran respectively.

-62-

The deoxybenzoin reaction product was compared with that obtained by  $Kresze^{57}$  from the treatment of deoxybenzoin with N-sulphinyl-p-toluenesulphonamide.

$$\frac{2PhCOCH_2Ph + 2CH_3C_6H_4SO_2NSO}{2PhCOCH_2Ph} \xrightarrow{A1C1_3} Ph S COPh + 2CH_3C_6H_4SO_2NH_2 + SO_2PhCOCH_2Ph}{PhCOCH_2Ph} + \frac{2CH_3C_6H_4SO_2NH_2 + SO_2PhCOCH_2PhCOCH_2PhC}{PhCOCH_2Ph} + \frac{2CH_3C_6H_4SO_2NH_2 + SO_2PhCOCH_2PhC}{PhCOCH_2Ph} + \frac{2CH_3C_6H_4SO_2NH_2 + SO_2PhC}{PhCOCH_2Ph} + \frac{2CH_3C_6H_4SO_2NH_2 + SO_2PhC}{PhCOCH_2PhC} + \frac{2CH_3C_6H_4SO_2NH_2 + SO_2PhC}{PhC} + \frac{2CH_3C$$

The configuration of the product from the deoxybenzoin/thionyl chloride reaction was largely trans, as indicated by its low melting point compared with the literature value of the cis-form<sup>45</sup>. The melting point of the trans-form is rather difficult to obtain accurately. Kresze only isolated an oil but Dittmer and Levy<sup>44</sup> obtained, after several attempts, a crystalline solid melting over a temperature range of  $6^{\circ}$ C. The oil obtained from the thionyl chloride reaction showed similar reluctance to crystallise although it did solidify on standing. It is reported that the n.m.r. spectrum of the cis-isomer shows a singlet whereas the trans-isomer gives a multiplet at  $\tau 2.34$ . The observed signal was a multiplet at  $\tau 1.90-2.55$ , confirming the lack of cis-isomer in any significant quantities. Dibenzoylstilbene was obtained when the thiiran was treated with triphenylphosphine. The other major product from this reaction was triphenylphosphine sulphide.

Tetraphenylthiiran was a product of the reaction of thionyl chloride with diphenylmethane, and was also found when chlorosulphinyldiphenylmethane was treated with thionyl chloride. It was present as a red oil after the sulphinyl chloride was distilled off. Unfortunately, other impurities stopped it crystallising from organic solvents and only a red oil separated from the cooling solution. Higher boiling solvents such as toluene seemed to cause a polymerisation reaction, as a product precipitated out of solution which was polymeric in nature.

-63-

Tetraphenylthiiran was prepared by a known route involving diphenyldiazomethane and sulphur<sup>60</sup>.

$$\frac{Ph}{Ph} + s \xrightarrow{Et_20} \frac{Ph}{Ph} \xrightarrow{C-C} \frac{Ph}{Ph} + N_2$$

The infra-red spectrum of the red oil and the authentic sample were similar, and thin-layer chromatography showed the two compounds to be identical. The red oil gave one spot and a small amount of residue that did not move with the solvent.

It was thought that di(acetylethoxycarbonyl)methyl sulphoxide was formed as an intermediate in the reaction between ethyl acetoacetate and thionyl chloride. It was hoped to prepare the sulphoxide and treat it with thionyl chloride to prove the point. Sulphoxides are usually prepared from sulphides by an oxidation process. Hydrogen peroxide is a common oxidising agent for this task but a danger exists in the oxidation of the sulphoxide one stage further to the sulphone. A large variety of oxidising agents are available which selectively give the sulphoxide. Some of these, as well as hydrogen peroxide, were tried but in all cases the attempts met with failure (Chapter 2.13). In no case was it possible to isolate the pure sulphoxide since the reactions were either reluctant to occur or went too far. The explanation is apparent when the mechanism of the oxidation is considered. In an article on oxidation at a sulphur atom 88 a general scheme was given in which the oxidation of sulphides by peroxides in an acidic or neutral medium involved nucleophilic attack by the sulphur atom on the oxygen-oxygen single bond of the peroxide. The sulphur atom donates a lone-pair of electrons to the oxygen atom in order to form a sulphur-oxygen bond. In di(acetylethoxycarbonyl)methyl sulphide there are electron-withdrawing substituents near the sulphur atom and, thus render it less likely to attack by an electrophile.

-64-

If alkaline conditions are used then the attacking species is a nucleophile which means that electron-withdrawing groups near the sulphur atom would increase the reaction rate. When a sulphoxide forms, however, the polarisation of the sulphur-oxygen bond is such that the sulphur atom becomes even more positive and is more susceptible to attack than the sulphide. Thus, a sulphone is formed in preference to a sulphoxide.

Disulphur dichloride was used to prepare compounds by known routes, as in several cases it gives the same product as the reaction of thionyl chloride with the compound in question. It was the similarity of the two reagents in this respect that led to the idea of an equilibrium existing between them.

 $2SOC1_2 \longrightarrow SC1_2 + SO_2C1_2$  $2SC1_2 \longrightarrow S_2C1_2 + C1_2$ 

Since sulphur dichloride decomposes on standing if stored without a stabiliser, it is reasonable to use disulphur dichloride because of its greater stability. Using disulphur dichloride under the conditions described (Chapter 2.5), it was possible to prepare alkenes from diethyl malonate and ethyl cyanoacetate, and a sulphide from ethyl acetoacetate. While attempting to prepare a disulphide of diethyl malonate, a method using disulphur dichloride was found<sup>68</sup>. Several attempts to repeat the work were made, but di(diethoxycarbonyl)methyl disulphide was never isolated. The oily product was mainly tetra-ethoxycarbonylethene. The same authors claim that dimethyl malonate gives a mixture of sulphide and trisulphide when treated in the same way as diethyl malonate. Once again their results were not repeatable, but a white solid was formed in good yield. Subsequent analysis indicated that the product was tetramethyl 1,2,4,5-tetrathian-3,3,6,6-

-65-

tetracarboxylate.

It is possible that an unsymmetrical ring was formed, i.e. tetramethyl 1,2,3,5-tetrathian-4,4,6,6-tetracarboxylate, but because the attacking species, disulphur dichloride, already contains a sulphur-sulphur bond the symmetrical structure seems most probable. Table 7 shows the main fragments obtained by mass spectrometry (see also Chapter 2, Fig. 3). The molecular ion peak (M) is easily seen at the position corresponding to a molecular weight of 388. The presence of sulphur in a molecule gives rise to a relatively large peak at M+2 because of the amount of  $^{34}$ S isotope present (4.4%) in naturally occurring sulphur. The compound tetramethyl 1,2,4,5-tetrathian-3,3,6,6-tetracarboxylate has the formula  $C_{10}H_{12}O_8S_4$ . Using the figures in Table 4 it can be shown that the calculated intensities of the M+1 and M+2 peaks are very close to the measured intensities (see following table). The molecular ion peak is arbitrarily assigned an intensity of 100.

Comparitive Intensities of Peaks at M, M+1, and M+2

Mass-to-charge ratio	Relative intensity			
	Calculated	Measured		
388 (M)	100	100		
389 (M+1)	14.32	14.1		
390 (M+2)	19.2	19.1		

There appears to be a difference between the reactions of thionyl chloride and disulphur dichloride with compounds containing an active methine group, e.g. 3-methylpentane-2,4-dione. This compound was prepared in the hope that its reaction with thionyl chloride would be slower than that of acetylacetone with thionyl chloride. Acetylacetone reacted rapidly to give an oil which could not be completely purified, although there was an indication that the product was some sort of polysulphide. When 3-methylpentane-2,4-dione was treated with thionyl chloride a red oil was obtained. An n.m.r. spectrum of the oil showed peaks attributable to the starting material and two new singlets at  $\tau 8.25$  and  $\tau 7.70$ . It is possible that the methine proton reacted with thionyl chloride to give a sulphinyl chloride. At the time further investigation was not thought necessary, but it is now suggested that the product formed was 3-chlorosulphinyl-3-methylpentane-2,4-dione.



The product was not the sulphide, as this compound, di(1,1'-diacetyl) ethyl sulphide, was prepared by treating 3-methylpentane-2,4-dione with disulphur dichloride. Analysis confirmed the structure as,



When ethyl  $\alpha$ -methylacetoacetate was treated with thionyl chloride at room temperature no reaction occurred. Heating for one hour at reflux temperature produced a red liquid which contained unchanged ester and another compound, probably ethyl  $\alpha$ -chlorosulphinyl- $\alpha$ methylacetoacetate.



The position of the  $\alpha$ -methyl protons in the n.m.r. spectrum had moved downfield to  $\tau$  8.20 and, as in the previous example, the loss of the methine proton resulted in the methyl peak changing from a doublet to a singlet. The acetyl protons also moved downfield to  $\tau$  7.65.

When treated with thionyl chloride under reflux conditions, ethyl  $\alpha$ -cyanopropionate gave a low yield of a compound which had an n.m.r. spectrum containing the expected ethyl triplet and quartet, but no other peak except a singlet at  $\tau$  8.1. Once again a sulphinyl chloride structure would fit very neatly, the proposed product being ethyl  $\alpha$ -chlorosulphinyl- $\alpha$ -cyanopropionate.

CH<sub>3</sub>CCO<sub>2</sub>Et SOC1

Before further analysis was possible the material started to darken and decompose. All attempts to repeat the experiment failed, however, because the ethyl  $\alpha$ -cyanopropionate did not react again with the thionyl chloride. It was not known then, that pure ethyl cyanoacetate does not react with thionyl chloride unless a catalytic quantity of anhydrous aluminium chloride is added. It is possible that the first reaction was catalysed by some impurity in the reaction vessel.

The identity of these proposed sulphinyl chlorides was never proven, but the evidence points strongly to the structures indicated above. Thionyl chloride has since been shown to give sulphinyl chlorides when treated with diphenylmethane (p. 21) and also a range of isopropyl ketones<sup>87</sup>.

The n.m.r. shift downfield of the methyl protons is, in each case, quite large and is shown in Table 8. This is in keeping with the electron-withdrawing nature of the chlorosulphinyl group and consequent de-shielding of the nearby protons. The effect is particularly noticeable in the shift of the  $\alpha$ -methyl absorption.

-68-

Table 8. The Positions of the n.m.r. Absorptions of the Proposed

Sulphinyl chlorides and their Parent Compounds	-
--	---

Parent Compound	τ Values				Sulphinyl Chloride
Service States	a	a'	Ъ	b'	
(a) CH_COCHCOCH_3 CH_3 (b)	7.90 (Keto) 7.80 (Enol)	7.70	8.75 (Keto) 8.15 (Enol)	8.25	(a') SOC1 CH <sub>3</sub> CO-C-COCH <sub>3</sub> CH <sub>3</sub> (b') $\overset{CH_3}{\overset{CH_3}{}}$
(a) CH <sub>3</sub> COCHCO <sub>2</sub> Et CH <sub>3</sub> (b)	7.80	7.65	8.75	8.20	$(a') \qquad \begin{array}{c} \text{SOC1} \\ \text{CH}_3 \text{CO-CCO}_2 \text{Et} \\ \text{CH}_3 \end{array}$
CNCHCO2Et CH3 (b)			8.45	8.10	SOC1 CN-C-CO <sub>2</sub> Et CH <sub>3</sub> (b')

The results of some experiments in Chapter 2 have a direct significance on the discussion of possible mechanisms and will be included in Chapter 5.

### Chapter 5

## DISCUSSION OF MECHANISTIC EXPERIMENTAL RESULTS

### 5.1. A General Reaction Mechanism

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It was shown earlier that the reaction of compounds containing active methylene groups with thionyl chloride gave a variety of different classes of compounds which, at first sight, seem unrelated. This chapter is devoted to showing how a similar mechanism can lead to several different products, and that alternatives to the proposed scheme do exist.

The first compound in this work treated with thionyl chloride was ethyl acetoacetate. As indicated in the introduction the expected product, ethyl 3-chlorocrotonate, was not obtained, but instead di(acetylethoxycarbonyl)methyl sulphide and ethyl α-chloroacetoacetate were formed. This fact indicated three possible reaction pathways, (a) two reactions proceeding in parallel, (b) a reaction proceeding through a single intermediate which then gave two products or, (c) a consecutive reaction in which one product was formed from the other.

Two parallel reactions may occur if there exists an equilibrium between thionyl chloride, sulphuryl chloride and sulphur dichloride.

	250012	$\Longrightarrow$ so <sub>2</sub> cl <sub>2</sub> + scl <sub>2</sub>	2	•	•	• •	•	a
and	2SC12 -	$\longrightarrow$ S <sub>2</sub> Cl <sub>2</sub> + Cl <sub>2</sub>						ъ

Equilibrium (a) has been postulated<sup>91</sup> whilst the sulphur chloride equilibrium (b) is well-known<sup>92</sup>. As di(acetylethoxycarbonyl)methyl sulphide may be prepared by the action of sulphur dichloride or disulphur dichloride on ethyl acetoacetate, while the  $\alpha$ -chloro compound is easily formed from the keto-ester and sulphuryl chloride, the proposed equilibrium may well explain the experimental results. At room temperature the equilibrium (a) is well over towards the left

-70-

and so it is usual to add copper powder to the system to act as a catalyst. However, even if only a small percentage of sulphuryl chloride and sulphur dichloride reacted with the ester, the equilibrium position would still be continually shifting from left to right. Although possible, the idea was discounted when the results of a reaction with a mixture of disulphur dichloride and sulphuryl chloride were obtained. The results are further discussed on p. 76.

It seems very likely that thionyl chloride itself is the attacking species and that it participates in an electrophilic attack on the enolic form of ethyl acetoacetate.



By analogy with an alcohol, the chloride atom of the chlorosulphite could attack the carbon atom of the double bond and give ethyl 3-chlorocrotonate.



This was not observed, but a similar attack by the sulphur atom would yield a sulphinyl chloride.



That this occurs is by no means certain and it may be argued that the enolic form could function similarly to an enol-ether, and hence,

thionyl chloride could add directly across the double bond.



This particular route is quite an attractive alternative to the chlorosulphite mechanism since the enolic species posseses a double bond suitably polarised to favour the suggested mode of attack by a positively charged species, i.e.



It is possible that ethyl  $\alpha$ -chlorosulphinylacetoacetate is an unstable intermediate which then reacts with another molecule of ethyl acetoacetate. Once again the reaction pathway is not clear-cut. If the chlorosulphinyl species attacks the electrophilic  $\alpha$ -carbon atom, a sulphoxide will be formed which could then be reduced to the sulphide by a molecule of thionyl chloride. A reduction of this type has been reported<sup>17</sup>, although no mechanism was proposed. The following scheme may now be suggested.

> · CH<sub>3</sub>COCHCO<sub>2</sub>Et + [CH<sub>3</sub>COCHCO<sub>2</sub>Et] H<sup>+</sup> -HCl , CH<sub>3</sub>COCHCO<sub>2</sub>Et -0 Cl , CH<sub>3</sub>COCHCO<sub>2</sub>Et] H<sup>+</sup> -HCl , CH<sub>3</sub>COCHCO<sub>2</sub>Et CH<sub>3</sub>COCHCO<sub>2</sub>Et , CH<sub>3</sub>COCHCO<sub>2</sub>Et

$$\underbrace{ \begin{array}{c} \text{SOC1}_2 \rightarrow \begin{bmatrix} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ +\$ - \text{O} - \$ \text{SOC1} \end{bmatrix} \text{C1}^- \xrightarrow{-\text{OSOC1}^+} & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- \xrightarrow{-\text{OSOC1}^+} & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_3 \text{COCHCO}_2 \text{Et} \end{bmatrix} \text{C1}^- & \begin{array}{c} \text{CH}_3 \text{COCHCO}_2 \text{Et} \\ \text{CH}_$$

When working with  $\beta$ -keto-sulphoxides, Russell<sup>21</sup> proposed that a chloride ion attacked the  $\alpha$ -carbon atom of the intermediate species and, by loss of hydrogen chloride and sulphur dioxide, an  $\alpha$ -chlorosulphide

-72-

was formed. Since the ethyl acetoacetate reaction produced no  $\alpha$ -chlorosulphide, an alternative scheme could involve the loss of a chlorosulphonyl cation followed by combination with a chloride ion to give sulphuryl chloride.

 $0SOC1^+ + C1^- \longrightarrow SO_2C1_2$ 

Formation of sulphuryl chloride in the last stage of the reaction would account for the formation of ethyl  $\alpha$ -chloroacetoacetate. Ethyl acetoacetate is present in larger quantities than the sulphide product during most of the reaction and so sulphuryl chloride will be more likely to react with the unchanged starting material.

If the sulphinyl chloride intermediate attacks another molecule of ethyl acetoacetate at the enclic oxygen rather than the  $\alpha$ -carbon atom, and the intermediate thus formed is attacked by a further molecule of thionyl chloride, the product will still be a sulphide and sulphuryl chloride.



 $\underbrace{\xrightarrow{\text{SOC1}}_{2 \to \left[ \begin{array}{c} \text{CH}_{3} \text{COCHCO}_{2} \text{Et} \\ \text{CH}_{3} \text{-} \begin{array}{c} \text{CH}_{3} \text{COCHCO}_{2} \text{Et} \\ \text{CH}_{3} \text{COCHCO}_{2} \text{Et} \end{array} \right] }$ 

The mechanism seems more probable because attack of an electrophilic sulphur atom on the lone pair of electrons of the oxygen atom will be preferable to nucleophilic attack by a carbanion that is present in very small quantities.

It was thought that blocking the hydroxyl group of the enolic tautomer, by replacing the hydrogen atom with an alkyl group, would

-73-

provide some useful information if such a compound was treated with thionyl chloride. If the reaction occurred by addition across the carbon-carbon double bond, then the reaction would proceed as before whereas attack at the hydroxyl group would be stopped. Ethyl 3-ethoxycrotonate, an enol ether, was prepared and treated with thionyl chloride. The reaction was rapid and a reddish-black tar was the only product obtained. Obviously the enol ether was reacting in a different manner from the normal enolic ester. Thus it may be concluded that ethyl acetoacetate probably reacts through the hydroxyl group of the enolic tautomer, the intermediate product being an unstable chlorosulphite as described earlier. The reaction is surprisingly slow when compared with some other reactions of thionyl chloride with compounds containing hydroxyl groups (e.g. alcohols). The slowest step is likely to be the formation of the enol. Ethyl acetoacetate can be isolated as the pure keto tautomer by distillation in a quartz apparatus and remains stable for some time if no acid or base is present to catalyse the tautomerisation. With this in mind it is feasible that thionyl chloride reacts with the enolic form as soon as it is formed but the rate determining step is the rate at which the enol becomes available for reaction. The sequence of the reaction is shown below.

 $\operatorname{CH}_3^{\operatorname{COCH}_2^{\operatorname{CO}_2^{\operatorname{Et}}}} \xrightarrow{\operatorname{Slow}} \operatorname{CH}_3^{\operatorname{C}=\operatorname{CHCO}_2^{\operatorname{Et}}}$ 

 $CH_{3C=CHCO_{2}Et} + SOC1_{2} \xrightarrow{Fast} CH_{3COCHCO_{2}Et} + HC1$ 

$$\begin{array}{c} \text{CH}_{3}\text{COCHCO}_{2}\text{Et} + \text{CH}_{3}\text{C=CHCO}_{2}\text{Et} + \text{SOC1}_{2} \xrightarrow{\text{Fast}} \xrightarrow{\text{CH}_{3}\text{COCHCO}_{2}\text{Et}} & \text{SO}_{2}\text{CL}_{2} + \text{HC1} \\ & \text{SOC1} & \text{SOC1} & \text{SOC1}_{2} & \text{CH}_{3}\text{COCHCO}_{2}\text{Et} & \text{SO}_{2}\text{CL}_{2} + \text{HC1} \\ & \text{CH}_{3}\text{COCHCO}_{2}\text{Et} & \text{SOC1}_{2} & \text{CH}_{3}\text{COCHCO}_{2}\text{Et} & \text{SOC1}_{2} & \text{CH}_{3}\text{COCHCO}_{2}\text{Et} & \text{SOC1}_{2} & \text{CH}_{3}\text{COCHCO}_{2}\text{Et} & \text{CH}_{3}\text{CH}_{3}\text{CH}_{3}\text{CH}_{3}\text{CH}_{3} & \text{CH}_{3}\text{CH}_{3} & \text{CH}_{3}\text{CH}_{3} & \text{CH}_{3} &$$

The idea is further substantiated by the observation that a catalytic quantity of pyridine markedly increases the rate of reaction. Pyridine

-74-

acts as a base and catalyses the tautomerism step. The rapidly formed enol then reacts with thionyl chloride before reverting back to the keto form. Thus the overall reaction is very much faster.

 $CH_{3}COCH_{2}CO_{2}Et + B \longrightarrow CH_{3}CO\overline{C}HCO_{2}Et + HB^{+}$  $CH_{3}C-\overline{C}HCO_{2}Et \longrightarrow CH_{3}C=CHCO_{2}Et$ 

 $CH_{3}C=CHCO_{2}Et + HB^{+} \longrightarrow CH_{3}C=CHCO_{2}Et + B$ 

B = a base, e.g. pyridine.

Ethyl  $\alpha$ -chloroacetoacetate is formed from di(acetylethoxycarbonyl) methyl sulphide by treatment with thionyl chloride at room temperature. The reaction is not clean and leads to a dark green oil from which the  $\alpha$ -chloro compound may be extracted. This reaction is not thought to be the main source of ethyl  $\alpha$ -chloroacetoacetate, as chlorination of the keto-ester by sulphuryl chloride, produced in the reaction, seems more likely. Although sulphuryl chloride reacts with the sulphide by removing both enolic protons, the rate is slow compared to the rate of reaction with ethyl acetoacetate. The formation of a green, and eventually black, oil in the thionyl chloride reaction mixture itself, clearly results from the decomposition of the sulphide in the presence of thionyl chloride. This also causes the low overall yield of sulphide (25-35%), as longer reaction times merely result in the decomposition of the sulphide.

It was found that both methyl and ethyl acetoacetate gave very similar products when treated with thionyl chloride and hence it was decided to study the reaction with other enolic compounds. The success with those compounds having a high enolic content was limited however. In most cases the reaction yielded complex tars, but there are indications that sulphides, polysulphides and sulphinyl chlorides

-75-

are formed with certain compounds<sup>87</sup>. Those compounds with low enol content, however, showed great potential and a study of the reaction of these compounds occupied the major part of this work.

It was found that ethyl cyanoacetate gave diethyl dicyanofumarate in good yields when treated with thionyl chloride, and that diethyl malonate also yielded the corresponding tetra-substituted alkene. Consideration of the list of compounds in Table 1 led to further investigation of various different compounds. The list of products obtained is given in Chapter 4 (Table 3).

There was still doubt as to whether the attacking species was thionyl chloride or some other sulphur chloride. The matter was resolved by taking a mixture of sulphuryl chloride and disulphur dichloride, and adding it to diethyl malonate. If disulphur dichloride reacted much faster than sulphuryl chloride, by adding 0.1 mole quantities of each reagent to 0.1 moles of diethyl malonate, no diethyl  $\alpha$ -chloromalonate would be formed and no information would have been obtained. The products did, in fact, include both the chlorinated compounds and tetraethoxycarbonylethene showing that sulphuryl chloride and disulphur dichloride react at fairly comparable rates. If an equilibrium existed between thionyl chloride and the above reagents there would inevitably be a similar mixture of products when diethyl malonate was treated with thionyl chloride. As only the tetrasubstituted alkene was obtained it may be concluded that it is formed as a direct result of attack by thionyl chloride on diethyl malonate.

It was not known if the reaction mechanism involved an enolic intermediate, since both ethyl cyanoacetate and diethyl malonate have measurable enol contents. It was found that both malononitrile and phenylacetonitrile yielded the appropriate alkenes on treatment with thionyl chloride. A keto-enol tautomerism is not possible in these cases but an imine may appear as the reactive species.

-76-

 $PhCH_2CN \longleftrightarrow PhC=C=NH$ 

Although a mechanism may be postulated for the preparation of a chlorosulphinyl intermediate via this route, it seems unlikely. Furthermore, the formation of a thiiran and a sulphinyl chloride, as probable reaction intermediates, from the treatment of diphenylmethane with thionyl chloride cannot take place via some form of tautomer. It would seem that the main requirement for reaction is a carbon-acid strength that is sufficient to allow thionyl chloride to remove a proton under the reaction conditions.

An interesting preparation of tetraethoxycarbonylethene from diethyl  $\alpha$ -bromomalonate and sodium trichloroacetate was reported by Krapcho and Huyffer<sup>93</sup>. They proposed a mechanism which could have been applicable to the thionyl chloride reactions and so it will be discussed briefly.

$$\operatorname{Br-CH}(\operatorname{CO}_{2}\operatorname{Et})_{2} + \operatorname{CCl}_{3}^{-} \longrightarrow \operatorname{Br-\overline{C}}(\operatorname{CO}_{2}\operatorname{Et})_{2} + \operatorname{CHCl}_{3}$$
$$\operatorname{Br-\overline{C}}(\operatorname{CO}_{2}\operatorname{Et})_{2} + \operatorname{BrCH}(\operatorname{CO}_{2}\operatorname{Et})_{2} \longrightarrow (\operatorname{EtO}_{2}\operatorname{C})_{2} \operatorname{C-C}(\operatorname{CO}_{2}\operatorname{Et})_{2} + \operatorname{Br}^{-}$$
$$\operatorname{EtO}_{2}\operatorname{C})_{2} \operatorname{C-C}(\operatorname{CO}_{2}\operatorname{Et})_{2} + \operatorname{CCl}_{3}^{-} \longrightarrow (\operatorname{EtO}_{2}\operatorname{C})_{2}\operatorname{C-C}(\operatorname{CO}_{2}\operatorname{Et})_{2} + \operatorname{CHCl}_{3} + \operatorname{Br}^{-}$$

()

A similar scheme could be proposed assuming thionyl chloride was able to act as a base in the same way as the trichloromethyl ion in this reaction. The second stage of the reaction would involve the formation of tetraethyl ethane-1,1,2,2-tetracarboxylate and the loss of a hydride ion. This is unlikely, as is the next step where a molecule of hydrogen would have to be eliminated rather than a molecule of hydrogen bromide. Before the idea was dismissed, however, the intermediate alkane was prepared by a known route and treated with thionyl chloride. No reaction occurred, as expected, and the mechanism was discounted as highly improbable.

The most feasible first step in the reaction is the formation of a sulphinyl chloride, but it is unlikely that it is produced by the reaction of thionyl chloride with a carbanion, formed from the starting compound by loss of a proton. i.e.

>CH2 -----> >CH + H + SOC12->>CHSOC1 + HC1

Several attempts were made to trap any such carbanion that was formed, by adding to the system a compound that readily forms a carbonium ion, for example, benzyl bromide or triphenylmethyl bromide. It was hoped that a compound resulting from the interaction of the oppositely charged ions would be recovered from the reaction mixture. For example, diethyl benzylmalonate would be found using benzyl bromide as the trapping agent.

 $(\text{Eto}_2\text{C})_2\text{CH}^- + \text{PhCH}_2^+ \longrightarrow (\text{Eto}_2\text{C})_2\text{CHCH}_2\text{Ph}$ 

Such a compound should be fairly easy to isolate from the rest of the reaction products and readily detectable by n.m.r. spectroscopy in the presence of other reaction products. Diethyl benzylmalonate would have two new absorptions in the region  $\tau$  6-7, one a triplet and the other a doublet. In no case was there any evidence for the existence of a carbanion intermediate.

Since no  $\alpha$ -substituted compounds were found it is reasonable to suggest that the carbanion does not exist as a capturable species. Thionyl chloride will be polarised,  $\operatorname{Cl}_2$ 5-0, and hence will probably attack the slightly negatively charged methylene group with subsequent loss of hydrogen chloride and formation of a sulphinyl chloride. Alternatively, the acidic proton may be removed by the oxygen atom of the thionyl chloride, followed by attack of the positively charged

-78-

sulphur atom of the protonated thionyl chloride on the methine group.

$$>_{CH_2} + SOC1_2 \longrightarrow >_{CH} + H-0-\overset{+}{5}-C1 \longrightarrow >_{CHSOC1} + HC1$$

It is envisaged that the two charged species exist together as an ion pair and hence no interaction with a carbonium ion can occur. The actual mechanistic pathway probably falls somewhere between the two alternatives and it would be unwise to propose one version in preference to the other.

There is little doubt that a sulphinyl chloride is the first formed intermediate. These compounds are well-known derivatives of sulphinic acids and have been prepared by a number of routes although, until now, it was common to use thionyl chloride only when it was desired to convert a sulphinic acid or its metal salt to a sulphinyl chloride. Although generally unstable in air and moisture, they are stable in a sealed tube at 5°C. It was not possible to detect a sulphinyl chloride in a reaction that yielded an alkene due, presumably, to its instability. However in cases where the sulphinyl chloride is relatively stable it may be isolated and this has been achieved in the reaction between diphenylmethane and thionyl chloride, and in some other work on isopropyl ketones<sup>87</sup>.

From the study of two sulphinyl chlorides, chlorosulphinyldiphenylmethane and methyl 2-chlorosulphinylpropionate, it was shown that the methine proton on the carbon atom adjacent to the chlorosulphinyl group appears at about  $\tau$  4-5.5 in the n.m.r. spectrum. By following the course of the reaction of ethyl cyanoacetate and thionyl chloride, using n.m.r. spectroscopy, it was hoped to detect a proton in this region. It turned out to be impossible, however, and only signals of the starting materials and the end product were observed. As it is probable that a sulphinyl chloride is an intermediate in the reaction, the reason for its non-appearance in the spectrum must be

-79-

due to its low concentration compared with the other compounds present.

The fact that only a low concentration of an intermediate is present can be explained in a logical qualitative way. If the intermediate is a reactive species then, naturally, it will react at a rate that is comparable to its rate of formation and, hence, very little will be present at any one time. It is possible to calculate the quantity of intermediate present in a series of consecutive reactions and a brief example is given here. The treatment is that given by Benson<sup>94</sup> for two consecutive second-order reactions. This particular case has been chosen because of the proposed E2 elimination of hydrogen chloride from a sulphinyl chloride to give a sulphine. If this postulate is incorrect then an alternative treatment is required but the presence of a low concentration of sulphinyl chloride can still be demonstrated. The reaction scheme may be written as

 $A + B \xrightarrow{k} 1 \rightarrow C$  $B + C \xrightarrow{k} 2 \rightarrow D$ 

A = methylene compound; B = thionyl chloride; C = sulphinyl chloride; D = sulphine;  $k_1$  and  $k_2$  are the rate constants. The following differential equations are then applicable

- $(1) \frac{dA}{dt} = -k_1 AB$
- (2)  $\frac{dB}{dt} = -k_1^{AB} k_2^{BC}$
- (3)  $\frac{dC}{dt} = k_1 AB k_2 BC = \frac{dB}{dt} \frac{2dA}{dt}$
- (4)  $\frac{dD}{dt} = k_2 BC = -\left[\frac{dB}{dt} \frac{dA}{dt}\right]$

The capital letters A, B, C and D are concentration terms. Using standard procedures, the four differential equations can be solved to give the expression

$$C = \frac{A}{K-1} \left[ 1 - \left( \frac{A}{A_0} \right)^{K-1} \right] \qquad \text{where } K = \frac{k_2}{k_1} \\ \text{and } A = A \text{ when } t = 0$$

The term  $A/A_{o}$  is related to the extent of the reaction, e.g. at the half-way point, half of the starting material will have been consumed, then,

$$A = \frac{1}{2}A_0$$

 $\frac{A}{A} = \frac{1}{2}$ 

and

By changing the value of  $A/A_o$  a series of values for CK/A can be obtained which, if plotted against the extent of reaction  $(1 - A/A_o)$ , result in a series of curves for different values of K (Fig. 9).

When  $k_2$  is considerably larger than  $k_1$  (K = 50) a constant value of CK/A is quickly reached and remains for the entire reaction. When K = 50, CK/A = 1.02 and C/A is approximately equal to 0.02. In real terms this means that the concentration of intermediate, C, is only 2% of the value of the concentration of starting material, A. Since starting material is being continuously consumed, to maintain a constant value of CK/A, the amount of intermediate will decrease along the flat part of the curve. As K decreases the amount of intermediate present at any one time increases and this may be seen by considering the curve for K=10 at the point where it cuts the curve for K=50. At that point exactly the same amount of A has been consumed and the ratio,CK/A is the same. i.e. when K = 50 and A = A<sup>1</sup>

then  $\frac{C_1K}{A^1} = \frac{50C_1}{A^1} = \text{constant}$ also when K = 10 and A = A<sup>1</sup>

then 
$$\frac{C_2K}{A^{\dagger}} = \frac{10C_2}{A^{\dagger}} = \text{constant}$$

therefore  $10C_2 = 50C_1$ 



Fig. 9 Concentration of intermediate in consecutive reactions.

If the calculation is continued then, when K = 1,  $(C = C_3)$  and K = 0.1,  $(C = C_4)$  for a particular value of CK/A, (Fig 9)

 $50.C_1 = 10C_2 = 1.8C_3 = 0.75C_4$ 

These figures indicate the marked increase in the concentration of an intermediate (relative to A) as K decreases, and it is only as the value of K begins to approach unity that the chance of detecting the intermediate becomes significant. When the sulphinyl chloride is relatively stable the second reaction.

 $B + C \xrightarrow{k_2} D$ 

will be much slower than the first so that  $k_1 \gg k_2$  and the intermediate, C, will increase in concentration and be the only product, i.e. the reaction will give a sulphinyl chloride and very little else.

On treatment with a base, usually triethylamine, sulphinyl chlorides lose hydrogen chloride to give compounds collectively known as sulphines.

>CH-SOC1 + Et<sub>3</sub>N  $\longrightarrow$  >C=S=0 + Et<sub>3</sub>N.HC1

This was originally shown by Sheppard<sup>95</sup> and has been enlarged upon by Strating et al.<sup>96</sup>. It is proposed here that thionyl chloride can act as a base towards the labile methine proton of the unstable sulphinyl chloride, and remove hydrogen chloride, probably in the form of an E2 elimination reaction.

 $H-0-\dot{S}Cl_2 + Cl^- \longrightarrow SOCl_2 + HCl$ 

It was reported by Sheppard<sup>95</sup> that the sulphine he prepared from 9-chlorosulphinylfluorene was unstable when heated, and at its melting point a large percentage of it gave 9,9'-difluorenylidene.



By analogy, it is reasonable to propose that a less stable sulphinyl chloride, such as those used in this study, might decompose readily at the temperature of refluxing thionyl chloride (80°C) to yield a tetra-substituted alkene.

Sulphines on treatment with certain compounds give adducts<sup>90</sup>; one such compound is 3,4,5,6-tetrachloro-1,2-benzoquinone which adds across the carbon-sulphur double bond.



It was thought that this principle could be applied to trap the sulphines proposed as intermediates in the thionyl chloride reactions. When a small amount of the benzoquinone (about 5% of the total weight of reactants) was added to a refluxing mixture of thionyl chloride and diethyl malonate the red colour of the benzoquinone disappeared within ten minutes. When a stoichiometric amount of benzoquinone was used, however, the red colour remained and the only isolatable compound different from the starting materials was tetrachlorocatechol. A possible explanation is that the experiment worked with a small quantity of quinone but that there was insufficient adduct to be isolated, whereas with larger amounts of quinone complications may

-83-

have arisen, altering the course of the reaction. Sulphines are reactive compounds and it is possible that two molecules will react with one another more rapidly than they react with any form of trapping species that is added to the reaction mixture. The harsh reaction conditions (thionyl chloride at 80°C) may decompose any adduct that happens to form; if a lower temperature could be used, success would be more likely.

When deoxybenzoin was treated with thionyl chloride it yielded a thiiran.

$$PhCOCH_2Ph + SOCI_2 \longrightarrow PhCO_C_Ph$$
  
 $PhCO_C_CPh$ 

This is precisely the same product as that obtained by Kresze<sup>57</sup> when he treated deoxybenzoin with p-toluene-N-sulphinylsulphonamide and anhydrous aluminium chloride.

 $CH_{3}C_{6}H_{4}SO_{2}N=S=0 + PhCOCH_{2}Ph \xrightarrow{A1C1_{3}} PhCO_{C} \xrightarrow{C} C \xrightarrow{Ph} + CH_{3}C_{6}H_{4}SO_{2}NH_{2}$ 

He proposed a reaction sequence in which a sulphine was initially formed and then dimerised to give a cyclic intermediate followed by loss of sulphur dioxide to yield a thiiran.

$$\begin{array}{ccccc} 2PhCCOPh & \longrightarrow & PhCO & Ph & & -SO \\ S & & Ph-C & C-COPh & & PhCO & C & C & Ph \\ O & & & S & O & & Ph & Ph & C & S & C & COPh \\ O & & & & S & O & & O \end{array}$$

The formation of a sulphine as an intermediate in this reaction is perfectly feasible since the sulphinyl structure (=S=0) is present at the beginning of the reaction and a simple scheme can be devised to show that it may be transferred to the deoxybenzoin structure. (Ar represents the group  $CH_3C_6H_4SO_2$ .)



If the two molecules of the sulphine dimerise, a cyclic structure will be formed which is unlikely to be very stable. Although the preparation of 2-oxo-1,2,5-oxadithiolans does not seem to have been reported, a slightly more stable ring, 2,5-dioxo-1,2,5-oxadithiolan or ethanedisulphinic anhydride, is known<sup>97</sup>.

The loss of sulphur dioxide from a 2-oxo-1,2,5-oxadithiolan resulting in a thiiran is a very likely event and it is envisaged as the next step in the reaction pathway. This type of reaction is well known<sup>98</sup> when the species being extruded is stable e.g. sulphur dioxide or carbon dioxide.

Another common extrusion reaction is that of sulphur from a thiiran to give an alkene, often accomplished by heating the material, although sometimes reagents such as triphenylphosphine are used. At the temperature of refluxing thionyl chloride (about  $80^{\circ}$ C) enough heat would probably be available to extrude sulphur from the thiiran to give an alkene. When the intermediate thiiran is stable, an alkene is not obtained from the reaction mixture. This is the case with diphenylmethane and deoxybenzoin, both of which yield thiirans on treatment with thionyl chloride.

There is also the possibility of a direct reaction between two molecules of a sulphine to form an alkene without passing through the oxadithiolan intermediate previously proposed. This entails the loss of two sulphinyl groups (S=0) which would disproportionate to sulphur

-85-

dioxide and sulphur. Sulphur monoxide (SO) is known to exist and disproportionate in this way. Its appearance in chemical reactions has been proved by trapping it with 2,3-diphenylbut-2-ene<sup>99</sup>. The following sequence is suggested to explain the appearance of an alkene.

$$\begin{array}{c} > C = S = 0 & -S0 \\ > C = S = \overline{0} & \longrightarrow \end{array} \end{array} \xrightarrow{> C = C <} S + S \\ \begin{array}{c} > C = S \\ > C = \overline{0} & \longrightarrow \end{array} \xrightarrow{> C = C <} S + S \\ \begin{array}{c} > S \\ > C = S \\ > C = S \\ \end{array} \xrightarrow{> C = C <} S \\ \begin{array}{c} > S \\ > S \\ > S \\ > S \\ \end{array} \xrightarrow{> C = C <} S \\ \begin{array}{c} > S \\ > S \\ > S \\ \end{array} \xrightarrow{> C = C <} S \\ \end{array}$$

Such a mechanism would explain the evolution of sulphur dioxide and loss of sulphur that occurs when alkenes are prepared, but it would not explain the production of thiirans. The possibility of the sulphines dimerising to give a four-membered ring (analogous to the dimerisation of ketene) has also been considered but will be dealt with in Section 5.4.

The evidence to suggest that sulphinyl chlorides and thiirans were reaction intermediates in the preparation of alkenes from thionyl chloride and compounds containing active methylene groups was not conclusive. It was decided that these intermediates should be prepared but, as described in Chapter 4, neither of them could be made from diethyl malonate or ethyl cyanoacetate for a variety of reasons. It was possible that the problem could be tackled in another way, namely the use of different starting materials.

The first compound used for the new approach was fluorene. It has already been described how an alkene was produced when 9-sulphinofluorene was heated. Since 9-chlorosulphinylfluorene is fairly easy to prepare, from 9-lithiofluorene and sulphur dioxide, it was decided to experiment with this. It was anticipated that treatment of 9-chlorosulphinylfluorene would yield either a thiiran or an alkene, or both.

-86-



Unfortunately, the sulphinyl chloride was too stable to react with thionyl chloride and so no further evidence for the theory was gained. It was not considered useful to prepare the sulphine, by treating the sulphinyl chloride with triethylamine, and then see the effect of thionyl chloride on the sulphine. It was already known that the alkene resulted from heating the sulphine <sup>95</sup>, and its preparation using thionyl chloride would not be a conclusive experiment.

It is known that thionyl chloride gives sulphoxides in some reactions and it was reported<sup>100</sup> that fluorene gave 9,9'-difluorenyl-sulphoxide when treated with thionyl chloride and anhydrous aluminium chloride.


If this was true, an interesting new reaction would have been open to investigation. The paper gave no experimental conditions and no yields. The evidence for the structure was a change in its melting point after treatment with hydrogen peroxide, presumably proof of an oxidation from a sulphoxide to a sulphone. Several attempts to repeat the preparation resulted in approximately 95% yields of a brown, infusible solid. The infra-red spectrum of the material indicated that it was a polymer but no further work was attempted on the reaction as it was deviating from the purpose of the experiment.

Having found that 9-chlorosulphinylfluorene did not react with thionyl chloride, another starting material was sought. The reason why a sulphinyl chloride had not been made from diethyl malonate was that both the thiol and the disulphide needed for the preparation were unstable. What was needed was a compound similar to diethyl or dimethyl malonate in some way, but that had a stable thiol; such a compound is methyl propionate. Replacement of one alkoxycarbonyl group by a methyl group is sufficient to stabilise the thiol and render the parent ester stable to treatment with thionyl chloride. Methyl 2-chlorosulphinylpropionate was prepared and treated with thionyl chloride under gentle reflux conditions for twenty-four hours. Subsequent analysis of the product showed that the major component was dimethyl dimethylfumarate. The scheme can be written as follows.

CH\_CH\_CO\_Me Several CH\_CHCO\_Me  $\xrightarrow{\text{SOC1}_2} \xrightarrow{\text{CH}_2\text{CCO}_2\text{Me}} \xrightarrow{\text{CH}_2\text{CCO}_2\text{Me}} \xrightarrow{\text{MeO}_2\text{CCCH}_2}$ 

Development of this particular route may be useful in synthesising tetra-substituted alkenes from compounds that do not react directly

-88-

with thionyl chloride.

The overall reaction sequence suggested for the preparation of alkenes from compounds containing active methylene groups by treatment with thionyl chloride is summarised below.

>CH2 + SOC12 -HC1 >>CHSOC1 -HC1 >>C=S=0

$$2 > c = S = 0 \longrightarrow s = s = s = s = 2 \longrightarrow c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c = c < s > c =$$

No single reaction has been found which shows every step described above, but enough evidence from several different reactions points to the series of events just discussed. When diphenylmethane is treated with thionyl chloride, the major product is chlorosulphinyldiphenylmethane. There is also a small amount of tetraphenylthiiran produced which can also be prepared treating chlorosulphinyldiphenylmethane with thionyl chloride.

$$Ph_2CH_2 + SOC1_2 \longrightarrow Ph_2CHSOC1 + \frac{Ph}{Ph} C_{Ph}$$
  
 $Ph_2CHSOC1 + SOC1_2 \longrightarrow$ 

It is thus reasonable to suppose that the sulphinyl chloride is a stable reaction intermediate in this particular case. The preparation of two thiirans, from deoxybenzoin and diphenylmethane, is a good indication that the proposed mechanism involves a thiiran intermediate even though it was not possible to prepare and treat the thiiran derived from diethyl dicyanofumarate. Methyl propionate was useful because its similarity to the malonates and cyanoacetates makes direct comparisons with such compounds more meaningful than, for example, the comparison of the reaction of thionyl chloride and diphenylmethane

-89-

with the reaction of thionyl chloride and dimethyl malonate. The reaction of 2-chlorosulphinylpropionate with thionyl chloride to give an alkene is a reasonable indication that other compounds containing active methylene groups react through sulphinyl chloride intermediates to give tetra-substituted alkenes.

The arguments put forward in this chapter, up to this point, have given a very strong indication that a particular reaction mechanism exists but the possibility of a free-radical mechanism has not been considered. This aspect of the work together with some proposals about the stereochemistry of the reactions will be dicussed in the following sections.

## 5.2. The Feasibility of a Free-Radical Reaction Mechanism

Up to this point it has been assumed that the reaction mechanism involves purely ionic steps but, in this section, the possibility that free-radicals play some part in the overall scheme will be discussed.

It is well-known that sulphuryl chloride is an efficient chlorinating agent and that it reacts by a free-radical mechanism. The overall equation for the chlorination of a saturated hydrocarbon is.

 $RH + SO_2Cl_2 \longrightarrow RCl + SO_2 + HCl$ 

The mechanism has been proposed to be similar to the chlorination of hydrocarbons by chlorine itself<sup>102</sup>.

$$SO_2Cl_2 \xrightarrow{\text{peroxide}} SO_2Cl \cdot + Cl \cdot$$
  
 $SO_2 + Cl \cdot$ 

 $RH + C1 \cdot \longrightarrow R \cdot + HC1$ 

 $R \cdot + SO_2Cl_2 \longrightarrow RCl + SO_2Cl \cdot$ 

The reaction is not quite as simple as this because sulphuryl

chloride has been shown to be a more selective chlorinating agent than chlorine. This has been attributed to the possibility of an equilibrium between the chlorosulphonyl radical, sulphur dioxide and the chlorine radical. The chlorosulphonyl radicals would then be present in solution as distinct species in addition to chlorine radicals and hence selectively abstract protons<sup>103</sup>.

S0, C1. \_\_\_\_ S0, + C1.

 $RH + SO_2C1^{\circ} \longrightarrow R^{\circ} + HC1 + SO_2$ 

R. + S0<sub>2</sub>C1<sub>2</sub> → RC1 + S0<sub>2</sub>C1.

Wyman et al.<sup>47</sup> have used sulphuryl chloride to chlorinate compounds containing active methylene groups. They explained their results by suggesting that the relative reactivity of such compounds towards sulphuryl chloride is enhanced by electron-withdrawing groups around the double-bond of an enolic intermediate, i.e.

 $\begin{array}{ccc} R-C-CH_2-R' & R' = electron-withdrawing \\ 0 & HO \\ \end{array}$ 

The double-bond is polarised in this way and the electron pair is localised towards the abstracting carbon atom. The reaction of compounds containing active methylene groups with sulphuryl chloride is considerably faster than the reaction of hydrocarbons with sulphuryl chloride under similar conditions. Hydrocarbons usually require treatment with sulphuryl chloride at reflux temperatures in the presence of a peroxide initiator whereas compounds containing active methylene groups require no peroxide to be added and room temperature is sufficient to bring about a reaction.

There is no obvious reason why thionyl chloride does not follow a similar route to sulphuryl chloride when added to compounds

-91-

containing active methylene groups. The first step would be the formation of chlorosulphinyl and chlorine radicals from thionyl chloride but then several alternative pathways are possible as shown below.

$$\operatorname{SOCl}_2 \longrightarrow \operatorname{SOCl} \cdot + \operatorname{Cl} \cdot \ldots$$
 (1)

$$R'-CH_2-R'' + Cl \cdot \longrightarrow R'-CH-R'' + HCl \quad ...(2a)$$

or 
$$R'-CH_2-R'' + SOCI \cdot \longrightarrow R'-CH-R'' + HSOCI \cdot \cdot \cdot (2b)$$
  
HCl + SO

then, 
$$R'-CH-R'' + SOCl_2 \longrightarrow R'-CH-R'' + SOCl_{(3a)}$$

or 
$$R'-CH-R'' + SOC1_2 \longrightarrow R'-CH-R'' + C1$$
 . . . (3b)  
SOC1

These steps seem quite feasible, but a number of arguments may be proposed against such a mechanism.

In equation (1), the initiation step, one of the differences between the thionyl chloride reaction and the sulphuryl chloride reaction lies in the nature of the products.

 $SOC1_2 \longrightarrow SOC1 \cdot + C1 \cdot \longrightarrow SO + 2C1 \cdot$ 

$$SO_{2}C1_{2} \longrightarrow SO_{2}C1 \cdot + C1 \cdot \longrightarrow SO_{2} + 2C1 \cdot$$

The change in enthalpy ( $\Delta H$ ) for the two reactions may be obtained using the published figures<sup>104</sup> for the enthalpies of formation ( $\Delta H_{f}$ ) of the reactants and products since,

$$\Delta H_{f}$$
 (products) -  $\Delta H_{f}$  (reactants) =  $\Delta H$ 

Thus, for thionyl chloride,

59.5 - (-59) = ΔH = 118.5 kcal/mole

and for sulphuryl chloride,

-12 - (-94) = AH = 82 kcal/mole

Hence, the sulphuryl chloride reaction is energetically more favourable because of the formation of the more stable sulphur dioxide molecule rather than sulphur monoxide.

If such a homolytic fission did occur in thionyl chloride, however, the next stages (2a and 2b) would be possible although equation (2b) is less likely because, once again, one of the products will be sulphur monoxide making the reaction less favourable than the equivalent step in the sulphuryl chloride reaction. The second propagation step involves either equation (3a) or (3b). The chlorine abstraction reaction (equation (3a)) suffers from the disadvantage of having sulphur monoxide as a product, but even so seems more feasible than the rather unusual substitution reaction of equation (3b).

Other reactions are likely to occur in the termination steps, e.g. the combination of two radicals.

This reaction, together with that in equation (3a), indicates that any free radical reaction occurring at this stage would almost certainly give rise to an  $\ll$ -chlorinated product as well as the sulphinyl chloride leading to the obtained alkene. Careful analysis of the reaction mixture from diethyl malonate and thionyl chloride showed no chlorinated compounds present. It was also found that very pure ethyl cyanoacetate did not react with thionyl chloride but the addition of aluminium chloride (only in catalytic quantities) started the reaction. This was useful in that it was a good indication that the initial stages

-93-

of the reaction were ionic. Further evidence was obtained by adding dibenzoyl peroxide to the reaction mixture. Peroxide did not initiate the reaction and thus it was assumed to be ionic rather than freeradical. It seemed fairly certain that the first stage of the reaction was formation of a chlorosulphinyl cation which went on to attack the active methylene compound as explained in the previous section.

$$\operatorname{SOCl}_2 + \operatorname{AlCl}_3 \longrightarrow [\operatorname{AlCl}_4]^{-} \operatorname{SOCl}^+$$
  
>CH<sub>2</sub> +  $[\operatorname{AlCl}_4]^{-} \operatorname{SOCl}^+ \longrightarrow > \operatorname{CHSOCl} + \operatorname{HCl} + \operatorname{AlCl}_3$ 

In an effort to induce a free-radical reaction, thionyl chloride and ethyl cyanoacetate were dissolved in redistilled decalin and heated at 100°C for twelve hours. It was thought that a high temperature and a non-polar solvent would favour a free-radical rather than an ionic reaction. Dibenzoyl peroxide was added to the stirred mixture but the only product isolated was diethyl dicyanofumarate. The products of the reaction were 95% unchanged starting materials and 5% of the alkene. As explained earlier, a radical reaction should give rise to some chlorinated products, but none was detected.

The experiments just described suggest an ionic mechanism for the formation of a sulphinyl chloride. The next steps in the proposed mechanism could still be free-radical however. Sulphur dioxide is evolved in the latter part of the reaction and the measure of the rate at which it is evolved from the solution was investigated.

If sulphur dioxide is evolved as a result of the following sequence,

$$> CHSOC1 \xrightarrow{-HC1} > C=S=0 \xrightarrow{>C=S=0} > C-C < \xrightarrow{-S0}_{2} > C-C < \xrightarrow{S}_{2} >$$

any change in the rate of reaction of the first two steps, brought

-94-

about by the addition of free-radical initiators or inhibitors to the reaction mixture, will be apparent from a study of the graphs of sulphur dioxide evolved plotted against time. The addition of a freeradical trap would result in an induction period caused by the intermediates combining with the radical trap. Once all the inhibitor: had been consumed, however, the reaction would proceed normally to evolve sulphur dioxide at the same rate as a non-inhibited reaction. The resulting graph would look something like that shown below.



The addition of a peroxide to the reaction mixture should have the opposite effect. The moment an intermediate is formed a radical species is present which is able to convert intermediates into reactive free-radicals. Thus, sulphur dioxide will be formed more rapidly as shown below.



-95-

As shown in Figs. 5 and 6 the addition of neither 2,3,5,6-tetrachloro-1,2-benzoquinone (chloranil) nor dibenzoyl peroxide had any effect on the sulphur dioxide evolution curves. Chloranil had to be used rather than the more usual inhibitors, e.g. benzoquinone, hydroquinone and phenols, because thionyl chloride reacts with such compounds, rendering them useless as inhibitors.

As a result of these experiments it was concluded that all the stages leading to the formation of sulphur dioxide were ionic in nature.

### 5.3. Discussion of Gas Evolution Experiments

The rate of evolution of gases from the straightforward reaction of ethyl cyanoacetate with thionyl chloride was measured as described in Chapter 3. No attempt was made to study the kinetics of the reaction in detail because of the complicated nature of the process. It is still not known what effect a solvent has on the reaction, and until a good method of following the kinetics is found, changing solvents and calculating rate constants from gas evolution studies will be of little value.

Measuring the amount of sulphur dioxide evolved from the reaction between ethyl cyanoacetate and thionyl chloride had another use apart from the free-radical work described in the previous section. Although difficult to imagine how the reaction could proceed without the evolution of sulphur dioxide, it was a possibility that had to be considered. The actual weight of sulphur dioxide evolved during the reaction was calculated from the iodine titrations and the figure was in close agreement with the theoretical weight. The yield of alkene was approximately 60%, and the yield of sulphur dioxide was within 5% of that figure on each occasion, the yield being calculated from the stoichiometric equation,

 $2CNCH_2CO_2Et + 2SOC1_2 \longrightarrow EtO_2C C=C CN + 4HC1 + SO_2 + S$ NC C=C CO\_2Et
-96-

The rate of evolution of hydrogen chloride was studied but little information was obtained because of the two-stage process in which it is produced, i.e.

> $>CH_2 + SOCl_2 \longrightarrow >CHSOCl + HCl$  $>CHSOCl \longrightarrow >C=S=0 + HCl$

It was considered worthwhile plotting the evolution of hydrogen chloride in some meaningful way, however, and so the rate of decrease of the active methylene compound was studied by converting the quantity of hydrogen chloride evolved into the amount of active methylene compound consumed. The assumptions that follow are only applicable at the beginning of the reaction before any significant amount of hydrogen chloride is lost from the sulphinyl chloride. The molar concentrations of ethyl cyanoacetate and thionyl chloride were almost equal, and were assumed to be so, at the beginning of the reaction and it was also assumed that the volume of the reaction mixture (V) did not change. Thus, if 'a' moles of each reactant were present initially, after a time, t, 'x' moles of hydrogen chloride will have been evolved and the concentrations of the reactants and products will be.

CNCH2C02Et + SOC12 ----> CNCH(SOC1)C02Et + HC1

$$\frac{(a-x)}{v}$$
  $\frac{(a-x)}{v}$   $\frac{x}{v}$   $\frac{x}{v}$ 

The rate equation for the production of a sulphinyl chloride is then,

$$\frac{d[CNCH(SOC1)CO_{2}Et]}{dt} = -\frac{d[CNCH_{2}CO_{2}Et]}{dt} = k[a-x]^{n}$$

V is an arbitrary volume and therefore may be assigned the value, 1. The rate constant is k, and the order of reaction is n.

It may be shown that for various reaction-orders, straight-line

relationships exist if certain functions of [a-x] are plotted against time. These are,

1st order;	ln[a-x] against t.
3/2 order;	$1/[a-x]^{\frac{1}{2}}$ against t.
2nd order;	1/[a-x] against t.

The plots for the 3/2-order and 2nd-order reactions are shown in Figs. 7 and 8, since these were in good agreement with a straight line. In each case the first seven points lie close to a straight line but the best agreement is the 3/2 order plot of  $1/[a-x]^{\frac{1}{2}}$  against time. After the seventh reading the points no longer lie on the straight line indicating that errors due to assumed constant volume of the solution, plus additional hydrogen chloride from the second part of the reaction, begin to markedly affect the results.

A straight line for a second order plot would mean that the following equation was true.

$$\frac{-d[a-x]}{dt} = k[a-x]^2$$

This may be put into real terms as,

$$\frac{d[CNCH_{CO_{2}Et]} = k[CNCH_{2}CO_{2}Et][SOC1_{2}]}{dt}$$

Ethyl cyanoacetate disappears in a reaction which is first order in both reactive species. The explanation is therefore in agreement with the mechanism already put forward i.e. electrophilic attack by the sulphur atom of thionyl chloride on the active methylene group.

The possibility of a 3/2 order does not rule out this reaction mechanism however. It is likely that an equilibrium step appears before the main reaction and the scheme is set out below.

$$\operatorname{SOCl}_2 \rightleftharpoons^{k}_1 \Longrightarrow \operatorname{SOCl}^+ + \operatorname{Cl}^- \dots \dots (1)$$

$$>CH_2 + SOC1^+ \xrightarrow{K} 2 \rightarrow >CHSOC1 + H^*$$
 , . . (2)

 $H^{+} + Cl^{-} \xrightarrow{k} 3 \rightarrow HCl \qquad \dots \qquad (3)$ 

It is assumed that the final formation of hydrogen chloride, equation (3), is fast and takes no part in any calculation of reaction order.

Now, 
$$-\frac{d [CNCH_2CO_2Et]}{dt^2} = k_2 [SOC1^+] [CNCH_2CO_2Et]$$

If equation (1) is an equilibrium step then the equilibrium constant,  $K = \frac{[\text{Socl}^+][\text{cl}^-]}{[\text{Socl}_2]}.$ 

Since the two ions SOC1<sup>+</sup> and C1<sup>-</sup> disappear at the same rate,  $[SOC1^+] = [C1^-]$ .

Then,

$$K = \frac{[SOC1^+]^2}{[SOC1_2]} \text{ or } [SOC1^+] = K^{\frac{1}{2}} [SOC1_2]^{\frac{1}{2}}$$

$$-\frac{d[CNCH_{2}CO_{2}Et]}{dt} = k_{2} k^{\frac{1}{2}} [SOC1_{2}]^{\frac{1}{2}} [CNCH_{2}CO_{2}Et]$$

i.e. the overall reaction is 3/2 order, but the formation of the sulphinyl chloride is still brought about by electrophilic attack of the sulphur atom on the active methylene group.

It is unreasonable to use these results to confirm conclusively a reaction scheme, but it is possible to use them to support rather than invalidate the proposed mechanism.

# 5.4. Stereochemical Consideration of the Formation of Alkenes using

## Thionyl Chloride Reagent

In some of the reactions of thionyl chloride with compounds containing active methylene groups, the products formed could have been the cisor trans-isomers of the particular product. This was the case with the alkenes formed by treating the cyanoacetates, phenylacetonitrile and methyl 2-chlorosulphinylpropionate with thionyl chloride. In the reaction with deoxybenzoin the product was a thiiran instead of an alkene, but it could still have had a cis- or trans-configuration. The assignment of a particular configuration to the structures actually prepared was discussed earlier and so the remarks made on the stereochemistry in the following paragraphs are of a more general nature.

In the reaction of ethyl cyanoacetate and thionyl chloride the major product of the reaction was diethyl dicyanofumarate (transisomer). When the progress of the reaction was followed using thinlayer chromatography, however, both diethyl dicyanofumarate and diethyl dicyanomaleate (cis-isomer) were detected. It was not possible to determine if one isomer was formed initially followed by partial isomerisation of the product or if both isomers were products of the reaction without any interference due to isomerisation occurring. The fact that the major product is the trans-isomer may be significant but, on the other hand, it is known that thionyl chloride catalyses the isomerisation of maleates to fumarates<sup>15</sup>.

If the reaction is stereospecific, the point at which the configuration is determined occurs when a cyclic intermediate is formed from two sulphines.



Hence the stereochemistry of the cyclisation process must be preceded by a brief discussion on steric effects in sulphines.

It is known that sulphines exist as cis- and trans-isomers<sup>105</sup>. i.e.





-100-

If the group that is cis to the oxygen atom is large, there is a possibility that there will be repulsion between that group and the oxygen atom. Such an isomer would be energetically less likely to exist than the form in which the bulky group is trans to the oxygen atom. If, in the two sulphines depicted above, substituent X is a cyano group and the other, Y, is an ethoxycarbonyl group, the linear nature of the cyano-group means that there is no possibility of any steric hindrance between it and the oxygen atom where they are cis to one another. This might not be the case when the ethoxycarbonyl group is cis to the oxygen atom and so stereochemical models were constructed to observe any steric effects. The bond distances for sulphines were taken from the literature<sup>106</sup>. The two isomers are represented below.





trans

Only in the case of the cis-isomer was there any close approach of the hydrogen atoms of the methyl group and the oxygen atom of the sulphine group. Close study of the stereochemical models suggests that steric repulsion is unlikely to be high enough to make one isomer less energetically favourable than the other. Hence the proportion of cis- to trans-sulphines formed would be approximately one to one with perhaps a slight excess of the trans-isomer. In the case where the ethoxycarbonyl group is replaced by a phenyl group, or even a methoxycarbonyl group, there would be no preference between the cisand trans-isomers.

Having established that there is no stereochemical reason why the two isomers of the sulphine should not be present in approximately

-101-

equal proportions, it is necessary to try to predict the way in which they will cyclise. It is envisaged that the first step is the formation of a new sulphur-oxygen bond which is formed by the combination of two sulphines as shown below.



The carbon-sulphur bonds both rotate through 90° to give the cyclic structure shown previously (p. 100).

The formation of an intermediate four-membered ring was considered but it is thought that the strained nature of the ring that would be formed made the process unlikely. The mechanism would have to be as follows (drawing an analogy with the formation of a ketene dimer).



Having decided that a five-membered ring is the most likely product, the nature of the ring closure can be discussed. To complete the ring the carbon atoms attached to the two sulphur atoms have to approach to within the distance of a chemical bond. If either of the groups X or Y is very bulky, this approach becomes rather difficult. Once again stereochemical models were used to simulate this process. The carbon-sulphur bonds have to rotate through 90° and the substituents X and Y move backwards so that the carbon atom may change from a planar ( $sp^2$ ) configuration to a tetrahedral ( $sp^3$ ) form. The direction of rotation of these groups may be predicted theoretically using the

-102-

Woodward-Hoffman rules 107 and will be dealt with shortly. The first requirement, however, is to see what effect various rotations have on the final configuration of the product. One form of rotation is when both bonds are rotated through  $90^{\circ}$  in the same direction (conrotatory motion) i.e.

$$X \xrightarrow{c} Y + X \xrightarrow{c} Y \xrightarrow{c} Y \xrightarrow{c} Y \xrightarrow{c} Y \xrightarrow{c} Y \xrightarrow{r} Y$$

Disrotatory is the opposite of conrotatory and the rotations are in opposite directions, i.e.

$$x \xrightarrow{\frown} C \xrightarrow{-} Y + x \xrightarrow{\frown} C \xrightarrow{-} Y \xrightarrow{-} y \xrightarrow{+} y \xrightarrow{+} x$$

If the effect of conrotatory motion is now shown on the semicyclised intermediates it can be seen that either a cis- or a transisomer may result.

Conrotatory motions



-103-

On elimination of sulphur dioxide the products in (a) and (b) would yield a cis-thiiran, and similarly (c) and (d) result in the transthiiran. It follows that disrotatory motion will give products as shown below.

cis sulphine + cis sulphine $\longrightarrow$	trans product	(e)
trans sulphine + trans sulphine $\longrightarrow$	trans product	(f)
cis sulphine + trans sulphine $\longrightarrow$	cis product	(g)
trans sulphine + cis sulphine	cis product	(h)

In the case where X is a cyano group and Y is an ethoxycarbonyl group there is a considerable amount of steric repulsion during the formation of the carbon-carbon bond, since both the groups lie in the same plane as the carbon atoms. Stereochemical models indicate that it is unlikely that two ethoxycarbonyl groups will be able to approach close enough to enable the carbon-carbon bond to be formed. Hence, the cis plus trans combination (c or g) is ruled out.



If two cis-sulphines (a or e) or two trans-sulphines (b or f) combined, the two interacting groups would be different and if only one group was bulky there would be less opposition to this process.



Both carbon-sulphur bonds would have to twist slightly so that one group was above and the other below the plane of the molecule. This is necessary to reduce steric interaction, to rehybridise to an sp<sup>3</sup> carbon atom, and hence to bring about the necessary condition for cyclisation to occur. Cyclisation in this way will lead to a cisproduct when conrotatory motion occurs and a trans-product for disrotatory.

The twisting action of the carbon-sulphur bonds just described is also necessary if two linear cyano groups interact (trans + cis cyclisation). However, the shape of this group is such that very little steric hindrance is possible, hence making this final alternative most likely. Viewing the structure from the side will give some indication of how such a process would work.



It can then be seen that the only process now possible is conrotatory motion about the carbon-sulphur bonds resulting in the trans product indicated in equation (d).

Although the most likely product of the reaction will be a transsubstituted ring there is a small chance that a cis-product will also form. Disrotatory motion is very unlikely with any combination of cisand trans-sulphines but conrotatory ring closure in equations (a) and (b) is possible and will yield a cis-product. This explains the small amount of cis-alkene that was detected in the reaction mixture.

Thus, in general terms the sulphines approach each other in such a manner that only the smaller groups sterically interact and ring closure is a conrotatory process with the smaller groups finishing in a trans-configuration with respect to one another.

The trans cyclic intermediate loses sulphur dioxide and sulphur

-105-

to yield an alkene and it is possible that some rotation about the carbon-carbon bond may occur during the alkene formation.



cis- and trans-alkenes

If the rotation about the carbon-carbon single bond is fast, compared with the loss of sulphur dioxide and sulphur and the formation of a new carbon-carbon double bond, then some isomerisation will inevitably occur. It seems probable however, that if such a process did occur, the most stable product would predominate, in this case the transalkene.

It was mentioned earlier that the preferred choice between disrotatory and conrotatory motion can be decided upon by application of the Woodward-Hoffman rules. In a thermally induced cyclisation, the allowed processes are disrotatory for a 4n + 2 pi-electron system and conrotatory for a 4n pi-electron system.

It is proposed that cyclisation of the two sulphine molecules occurs by the formation of a sulphur-oxygen bond followed by the attack of one carbon atom on another to close the ring. The major assumption in this argument is that the electronic structure of the non-cyclised intermediate does not have time to change significantly compared with the parent sulphines. This enables a large degree of pi-electron delocalisation to exist before the formation of the new carbon-carbon bond. The five atoms that constitute the ring may then be said to be  $sp^2$  hybridised, leaving eight pi-electrons delocalised around the ring. The difference in polarity of the two carbon atoms (see diagram, p. 102) will be minimised to a large extent and the Woodward-Hoffman rules then predict a thermal conrotatory cyclisation. This is exactly the same

-106-

conclusion as was drawn from the previous paragraphs based purely on stereochemical considerations.

The alternative to attack of the oxygen atom on a sulphur atom, as the initial step in a cyclisation process, is a 3 + 2 cycloaddition reaction.



Such a process was not considered possible for two reasons however. Firstly, the polar nature of the sulphines makes it much more likely that electrophilic attack of the sulphur atom on the oxygen will occur before a concerted cycloaddition is possible. Secondly, such a process involves six pi-electrons allowing a disrotatory thermal ring closure, and this has already been shown to be stereochemically unfavourable.

A very simple Huckel Molecular Orbital treatment of the semicyclised system confirms that a conrotatory process is feasible. The procedure used is outlined in a book by Murrel, Kettle and Tedder<sup>108</sup>. Using their assumptions and symbols a set of secular equations may be obtained for the system shown below.

	6	1	1		1	-
6-30	Õ	Ũ	0	0	U	-
	(1)	(2)	(3)	(4)	(5)	

$(\mu = 1)$	$xc_1 + c_2$	= 0
$(\mu = 2)$	$C_1 + xC_2 + C_3$	= 0
$(\mu = 3)$	$C_2 + xC_3 + C_4$	= 0
$(\mu = 4)$	$c_3 + xc_4 + c_5$	= 0
$(\mu = 5)$	$C_4 + xC_5$	= 0

-107-

$$x = \alpha - E \beta$$

 $\ll$  = Coulomb integral  $\beta$  = Resonance integral E = pi-energy integral

 $\propto$  and  $\beta$  are defined for benzene, but in a system containing heteroatoms these values have to be modified. For an atom X bound to a carbon atom the following equations apply.

> $\alpha_{x} = \alpha_{c} + h_{x}\beta_{c-c}$  $\beta_{c-x} = k_{c-x}\beta_{c-c}$

The values of  $h_x$  and  $k_{c-x}$  were obtained from the literature<sup>109</sup> and the following secular determinant was then used to solve the set of equations above.

x	0.8	0	0	0	
0.8	x	0.5	0	0	1.100
0	0.5	x+1	0.5	0	= 0
0	0	0.5	x	0.8	
· 0	0	0	0.8	x	

For a general case  $\psi_i = \xi_{rir}^{C} \phi_r$ .

Solving the determinant provided the following equations.

$$\begin{split} \Psi_1 &= 0.21 \not p_1 + 0.38 \not p_2 + 0.79 \not p_3 + 0.38 \not p_4 + 0.21 \not p_5; & E = \alpha + 1.47 \beta \\ \Psi_2 &= -0.5 \not p_1 - 0.50 \not p_2 &+ 0.50 \not p_4 + 0.50 \not p_5; & E = \alpha + 0.8 \beta \\ \Psi_3 &= 0.5 \not p_1 + 0.29 \not p_2 - 0.55 \not p_3 + 0.29 \not p_4 + 0.51 \not p_5; & E = \alpha + 0.46 \beta \\ \Psi_4 &= -0.5 \not p_1 + 0.5 \not p_2 &- 0.56 \not p_4 + 0.5 \not p_5; & E = \alpha - 0.8 \beta \\ \Psi_5 &= -0.4 \not p_1 + 0.52 \not p_2 - 0.26 \not p_3 + 0.52 \not p_4 - 0.44 \not p_5; & E = \alpha - 0.9 \beta \end{split}$$

The molecular orbitals may be represented diagramatically as follows.





There are eight pi-electrons in the systems and so if each orbital is filled (two electrons) then only the first four orbitals will be occupied. The Woodward-Hoffman rules are decided upon by considering the highest energy orbital that is occupied, in this case  $\psi_A$ .



Only conrotatory cyclisation will lead to a situation in which there is a positive overlap and hence formation of a new sigma-bond. The process is accompanied by a change of hybridisation of the carbon atom from  $sp^2$  to  $sp^3$ .

i.e.



Thus, the combination of a trans- and a cis-sulphine has again been shown to yield a trans-product.

### Chapter 6

### CONCLUSION

The initial investigations carried out in this work were in many ways purely exploratory. It was found that the products of the reaction of thionyl chloride and compounds containing active methylene groups were dependant on the degree of keto-enol tautomerism exhibited by a particular compound. In compounds where the enol content was greater than about two percent the products were usually sulphides. This aspect of the work was not fully investigated but became the subject of a separate Ph.D. thesis<sup>110</sup>.

In compounds containing less than one percent of enol-tautomer it was found that an alkene resulted on treatment with thionyl chloride. The reaction was developed into a useful synthesis of tetra-substituted alkenes<sup>111</sup>. There is room for further development of the indirect route in which sulphinyl chlorides may be prepared by known methods and then treated with thionyl chloride to yield alkenes, and also the use of thionyl chloride to prepare sulphinyl chlorides directly in one step.

The mechanism of the reaction in which sulphides are prepared remains speculative as little time was spent on this topic. The mechanism of the formation of alkenes has been proposed with considerably more certainty however. The postulated mechanism has been fully discussed in Chapter 5 but some element of doubt about the exact route must inevitably remain until a complete study of the reaction kinetics has been made. A reliable technique of following each step of the reaction is required and this would allow a study of the effect of solvents and temperature on the reaction. The effect of catalysts such as aluminium chloride and pyridine will also have to be investigated to give a complete picture of what is going on. It would be useful to find a structure which is able to produce either a

-111-

sulphide or an alkene, depending on the reaction conditions, when treated with thionyl chloride.

When the reaction is thoroughly understood it will be possible to predict which particular reaction product will be obtained and also help in indicating the optimum reaction conditions. It is this last point which will be most valuable since the usefulness of thionyl chloride as a synthetic reagent is at present limited because of its tendency to produce intractable tars in the presence of some organic compounds.

# Appendix I

Di	gico Micro 16 Program for Calculating the Weight of Sulphur Dioxide
Ev	olved (see Section 3.2.1.).
10	ASK I,S
20	SET S1=0
30	SET VOL=51
40	TYPE! " X SO SI+SO",!
50	ASK X; IF (X),120,120,60
60	SET NEW I=X*S/10
70	SET VOL=VOL-1
80	SET SO=(32*VOL*(1-NEW I))/100
90	SET I=NEW I
100	TYPE % 5.04," ",S0," ",S0+S1,!
110	SET S1=S0+S1
115	GO 50
120	QUIT

I = Normality of iodine solution.

S = Normality of sodium thiosulphate solution.

X = Volume of sodium thiosulphate.

# Appendix II

Digico Micro 16 Program for Calculating the Weight of Hydrogen
Chloride Evolved (see Section 3.2.2.).
10 ASK Y,Z
20 SET HC1=0; SET N1=0; SET V=505
25 TYPE! "KCNS AGNO3 HC1/ALI TOT HC1 LOG 1/HC1 "
28 ASK D
29 TYPE: ;ASK(0)C; TYPE % 3.02,! C
30 SET C=C+0.05; IF(C),110,28,31
31 SET P=-2; SET V=V-5
32 SET P=P+1; IF(P),34,35,36
34 GO 40
35 SET C=C-0.1; TYPE!," ";GO 40
36 SET C=C+0.05; TYPE!," ";G040
40 SET Y1=(C*Y)/Z; TYPE "
50 SET Y2=D-Y1
60 SET N2=(Y2*Z)/5
70 SET H2=(N2-N1)*36.48*(V/1000)
80 TYPE % 5.04," ",H2," ",H2+HC1," ",FLOG(H2+HC1),"
85 TYPE 1/(H2+HC1)
90 IF(P-1), 32, 100, 100
100 SET HC1=H2+HC1; SET N1=N2; GO 29
110 QUIT
Y = Normality of potassium thiocyanate solution.
Z = Normality of silver nitrate solution

tt

- D = Volume of silver nitrate solution.
- C = Volume of potassium thiocyanate solution.

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-117-

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### ADDENDA

The information supplied in Chapters Two and Three is, in some cases, incomplete. In order to provide a more unambiguous characterisation of some of the compounds prepared, and to supply some additional quantitative data, the following remarks should be read in conjunction with the indicated sections.

### Chapter 2

## Preparation of 1,2-Diphenylethene-1,2-dicarbonitrile (p. 16)

The mass spectrum showed a molecular ion peak at 230 (molecular weight of 1,2-diphenylethene-1,2-dicarbonitrile is 230). Using the values in Table 4 (p. 57) the M+1 peak was calculated to be 18.51% for  $C_{16}H_{10}N_2$ . The experimental value was 17.30%. Preparation of Di(acetylethoxycarbonyl)methyl sulphide (p. 17)

The solid compound prepared from the reaction between ethyl acetoacetate and thionyl chloride has been shown (by spectral analysis) to be identical to the product prepared from the action of disulphur dichloride on ethyl acetoacetate. Both elemental analysis (C, 50.0%; H, 6.3%; calculated for  $C_{12}H_{18}O_6S$ ; C, 49.6%; H, 6.3%) and mass spectral data, given below, point to the compound being a sulphide rather than the expected sulphoxide (calc. for  $C_{12}H_{18}O_7S$ ; C, 47.0%; H, 5.9%). In addition the formation of a sulphoxide by the treatment of a keto-ester with disulphur dichloride is unlikely.

The molecular ion peak at 290 corresponds to the structure,

сн<sub>3</sub>соснсо<sub>2</sub>с<sub>2</sub>н<sub>5</sub> s сн<sub>3</sub>соснсо<sub>2</sub>с<sub>2</sub>н<sub>5</sub>

-1-

Main Fragments of the Mass Spectrum of Di(acetylethoxycarbonyl)methyl

Sulphide

Mass-to- Charge Ratio	Relative Intensity	Nature of Fragment	
290	5	(CH3COCHCO2Et)2S	
248	3.5	(CH2CO2Et)S(CH3COCHCO2Et)	
202	30	(CH2COH)S(CH2COCHCO2Et)	
156	18	(CHCO)S(CH <sub>3</sub> COCCO)	
130	7	CH3COCH2CO2Et	
85	17	C.COOEt	
60	10	S-C0	
45	48	с <sub>2</sub> н <sub>5</sub> 0	
43	100	снзсо	

Using the figures in Table 4 (p. 57) the intensities of the M+1 and M+2 peaks (M = molecular ion peak) for  $C_{12}H_{18}O_6S$  were calculated. These are shown below with the experimental figures.

M+2	M+1	М	
6.7	13.5	100	Calculated
5.6	14.1	100	Found
	14.1	100	Found

The other product of the reaction between ethyl acetoacetate and thionyl chloride was shown to be ethyl  $\ll$ -chloroacetoacetate. In addition to n.m.r. data, the distillate was analysed by gas-liquid chromatography. The solutions compared were as follows,

(a) ethyl acetoacetate

(b) ethyl &-chloroacetoacetate (see Addenda p. 7)

- (c) ethyl «, «-dichloroacetoacetate (see Addenda p. 7)
- (d) ethyl B-chlorocrotonate (see Addenda p. 8)
- (e) distillate from the reaction mixture of ethyl acetoacetate (1 mole) and thionyl chloride (1 mole)
- (f) distillate from the reaction mixture of ethyl acetoacetate(2 moles) and thionyl chloride (1 mole)

Using an SE30 column (9 ft) at  $180^{\circ}$ C the following retention times were obtained.

Solution	Retention Time (minutes)				
Stranger and	1	2	3	4	5
(a)	21	3	-	-	-
(b)	-			5	-
(c)	-	-		-	63/4
(d)	- 10	- 10	3불	-	-
(e)	24	3(19%)	-	5(81%)	-
(f)	21/4	3(64%)	-	5(36%)	-

### Key to columns

- 1 = Ethyl acetoacetate (enol)
- 2 = Ethyl acetoacetate (keto)
- 3 = Ethyl B-chlorocrotonate
- 4 = Ethyl <-chloroacetoacetate
- $5 = \text{Ethyl} \propto, \propto -\text{dichloroacetoacetate}$

The percentage composition (figures in brackets) of ethyl acetoacetate in solutions (e) and (f) includes the keto and enol tautomers as one compound. The addition of ethyl  $\propto$ -chloroacetoacetate to solutions (e) and (f) and running a g.l.c. on the mixture resulted in no new peaks, whereas ethyl  $\beta$ -chlorocrotonate gave a distinct peak when added to solutions (e) and (f).
#### A typical chromatogram is shown below.



Time (minutes)  $\rightarrow$ 

Comparison of the n.m.r. spectra of ethyl  $\prec$ -chloroacetoacetate and ethyl  $\beta$ -chlorocrotonate shows that the two compounds cannot be confused.

Ethyl  $\propto$ -chloroacetoacetate. CH<sub>3</sub>COCHCO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>CH<sub>3</sub>

Triplet 78.70 Ethyl protons Quartet 75.70

Singlet ~7.65 Acetyl protons

Singlet ~ 5.00 Proton adjacent to chlorine atom

Ethyl B-chlorocrotonate.





trans

cis

Triplet 78.75 Quartet 75.80) Singlet 77.75 Methyl protons (trans) Singlet 77.45 Methyl protons (cis) Singlet 74.00 Vinyl proton (trans) Singlet 73.95 Vinyl proton (cis)

The assignment is in agreement with published data 112.

-4-

# Preparation of trans-Dibenzoylstilbene (p. 20)

In addition to trans-dibenzoylstilbene, triphenylphosphine sulphide (Ph<sub>3</sub>PS) was isolated from the reaction mixture. It was characterised by its melting point, 158-9°C (Lit. 157.5°C)<sup>113</sup>, and its infrared spectrum, which was in agreement with published data<sup>115</sup>. <u>Preparation of Chlorosulphinyldiphenylmethane</u> (p. 21)

The first fraction was shown to be unchanged diphenylmethane by comparing its n.m.r. and i.r. spectra with a known sample (Lit. b.p. 125°C at 10 mmHg)<sup>116</sup>.

The n.m.r. spectrum of the sulphinyl chloride product (which showed it to be>95% pure) could have been misinterpreted, since chlorodiphenylmethane may have given a similar spectrum. The published data<sup>114</sup> for the latter compound shows this not to be the case.



(a) is a Singlet at 7 3.80

(b) is a Multiplet at  $72.67 \pm 0.05$ 

Reaction of Thionyl Chloride with Ethyl 2-cyanopropionate (p. 23)

Spectral (i.r. and n.m.r.) and g.l.c. analysis showed the first fraction to be identical to ethyl 2-cyanopropionate (p. 30). Methyl 2-chlorosulphinylpropionate (p. 25)

In addition to the n.m.r. evidence for the formation of dimethyl dimethylfumarate, the infrared spectrum of the product provides a further pointer to the structure.

i.r. (thin film): 2990(m), 2960(m), 2930(w), 1730(s), 1440(s),

1290(s), 1210(s), 1030(s), 950(m), 855(m)cm<sup>-1</sup>.

Dimethyl fumarate<sup>115</sup>.  $\gamma$  max 1721, 1441, 1312, 1163, 990 cm<sup>-1</sup>. The loss of the strong peak at 1150 cm<sup>-1</sup> indicates that the chlorosulphinyl group is absent.

-5-

#### Preparation of Diethyl Dicyanofumarate (p. 27)

It is possible that a sulphur containing compound could result from the reaction between ethyl cyanoacetate and disulphur dichloride. A Lassaigne sodium fusion test, however, proved negative with respect to sulphur. Naik named his product as diethyl dicyanosuccinate  $(C_2H_5O_2CCH(CN)-CH(CN)CO_2C_2H_5)$  but this assignment was shown to be incorrect by the lack of a methine singlet in the n.m.r. spectrum at about 76 (e.g. tetraethoxycarbonylethane has a methine singlet at 76.05).

Preparation of Di(acetylethoxycarbonyl)methyl sulphide (p. 28)

Disulphur dichloride is a known reagent used for the preparation of sulphides. Despite the discrepancy between the literature and found melting points it is difficult to envisage anything other than a sulphide (e.g. sulphoxide) being prepared. The infrared and n.m.r. spectra of this compound were identical to those of the product from the ethyl acetoacetate/thionyl chloride reaction (p. 17). The mass spectrum of the product has also been shown to agree with that expected from the postulated sulphide (Addenda p. 2). The infrared spectrum shows a peak at 1060 cm<sup>-1</sup> which is also present in di(acetylmethoxycarbonyl)methyl sulphide. This single isolated peak is also present in ethyl acetoacetate (1050 cm<sup>-1</sup>) and is assigned to C-0 stretching in an ester group, and not to S=0 stretching in a sulphoxide.

Reactions of Sulphuryl Chloride (SO\_C1\_) (p. 29)

(a) Diethyl «-chloromalonate.

The procedure was the same as that used by Wyman<sup>47</sup>, and the product was a pure (g.l.c) colourless liquid. b.p. 130-2°C at 25 mmHg, (Lit. 127-8°C at 20 mm Hg)<sup>47</sup>. n.m.r. (CCl<sub>4</sub>): Triplet 78.70 6 protons Quartet 75.75 4 protons Singlet 75.00 1 proton

-6-

(b) Ethyl a-chloroacetoacetate

Fractional distillation of the reaction mixture of ethyl acetoacetate (1 mole) and sulphuryl chloride (1 mole) provided a pure sample of ethyl  $\propto$ -chloroacetoacetate. b.p. 44-6°C at 5 mmHg (Lit. 94-6°C at 30 mmHg)<sup>47</sup>.

n.m.r. (CCl<sub>4</sub>): Triplet 28.70 3 protons Singlet 27.65 3 protons Quartet 25.70 2 protons Singlet 25.00 1 proton

(c) Ethyl & -dichloroacetoacetate

Using ethyl acetoacetate (1 mole) and sulphuryl chloride (2 moles) ethyl  $q_{q}$ -dichloroacetoacetate was obtained. b.p. 58-60°C at 5 mmHg. (Lit. 106-8°C at 30 mmHg)<sup>47</sup>.

n.m.r. (CCl<sub>4</sub>): Triplet 78.65 3 protons Singlet 77.55 3 protons Quartet 75.60 2 protons

Both samples (b and c) were checked for purity by g.l.c. using the conditions on page two of the Addenda.

Preparation of 3-Methylpentane-2,4-dione (p. 29)

The literature values of the boiling point of the dione are  $68-70^{\circ}C$  at 26 mmHg<sup>48</sup> and  $170-72^{\circ}C^{49}$ .

Preparation of Ethyl <-methylacetoacetate (p. 30) Literature<sup>116</sup> b.p. 187°C.

Preparation of Ethyl 2-cyanopropionate (p. 30) Literature<sup>50</sup> b.p. 77°C at 9.5 mmHg. Preparation of 3,3-Dimethylpentane-2,4-dione (p. 31) Literature<sup>116</sup> b.p. 173°C.

Preparation of t-Butyl cyanoacetate (p. 31) Literature b.p. 67-8°C at 1.5 mmHg<sup>53</sup>.

-7-

### Preparation of Ethyl 3-ethoxycrotonate (p. 32)

The first stage of the synthesis involved the preparation of ethyl 3-chlorocrotonate. b.p.  $50-65^{\circ}C$  at 10 mmHg. (Lit. b.p. cis,  $48.5^{\circ}C$  at 10 mmHg, trans,  $69.5^{\circ}$  at 10 mmHg)<sup>26</sup>. The n.m.r. spectrum and g.l.c. analysis of this compound were given on the third page of the Addenda.

Ethyl 3-ethoxycrotonate (Lit. m.p. 30.2°C)<sup>26</sup> was prepared from the chlorocrotonate.

## Preparation of 9-Chlorosulphinylfluorene (p. 33)

The product of the reaction absorbs strongly at 1150 cm<sup>-1</sup> which is indicative of a sulphinyl chloride.

# Preparation of 2,3-Epithio-1,2,3,4-tetraphenylbutane -1,4-dione (p. 34)

The product was purified by eluting the oily product through a silica-gel column with benzene. Pale yellow crystals, m.p.  $95-97^{\circ}C$  (Lit. m.p.  $104-5^{\circ}$ )<sup>57</sup>. The infrared spectrum was identical to that of the product from the thionyl chloride/deoxybenzoin reaction.  $\mathcal{Y}$  max =  $3070 \text{ cm}^{-1}$ , aromatic hydrogen atoms;  $1680 \text{ cm}^{-1}$ , Ph-C=O; 1600, 1580,  $1455 \text{ cm}^{-1}$ , aromatic C=C stretching;  $1215 \text{ cm}^{-1}$ , aromatic ketone (C-O stretch).

The mass spectrum was of little use since no molecular ion peak was visible. The main peaks were,

m/e	Relative Intensity	Structure
210	2.5	PhCO, COPh
105	100	PhCO
77	58	Ph
51	64	C4H3

There were no peaks between 105 and 210.

-8-

# Preparation of Tetraphenylthiiran (p. 34)

Investigation of the product by t.l.c. using two solvents of different polarity (p. 21) showed the compound to be pure. <u>Preparation of Methyl 2-mercaptomalonate</u> (p. 36)

Boiling point of the product, 50-51°C at 20 mmHg. (Lit. b.p. 44-6°C at 15 mmHg)<sup>64</sup>.

Chapter 3

### Section 3.2.3 (p. 45)

### Sulphur Dioxide

The graphs that were plotted (Figs. 5 and 6) to show the weight of sulphur dioxide evolved from the reaction mixtures were derived from the calculation of titration results (Appendix I). To obtain the weight of sulphur dioxide that was attributable to thionyl chloride being swept over, a 'blank' determination was carried out. The figures shown in the Table A below were plotted in Figure 5 and are approximate to seen to be a straight line.

Volume of $Na_2S_2O_3$ (cm <sup>3</sup> )	Weight of SO <sub>2</sub> (g)	Time (hours)
15.90	0.0225	1/3
15.80	0.0383	23
15.60	0.0694	1
15.55	0.0770	13
15.50	0.0844	1윻
15.40	0.0989	2
15.40	0.0989	23
15.20	0.1267	23
15.10	0.1403	3
15.00	0.1536	3=3
15.00	0.1536	38

Table A. Sulphur Dioxide Derived from Thionyl Chloride

-9-

Normality of iodine solution (I) = 0.162

Normality of sodium thiosulphate solution (S) = 0.101

In order to obtain the exact weight of sulphur dioxide evolved from the other reactions, the weight of sulphur dioxide from the 'blank' would have to be subtracted. When either tetrachloro-p-benzoquinone or dibenzoyl peroxide was added to the reaction mixture the blank was the ethyl cyanoacetate/thionyl chloride reaction since only a comparison of sulphur dioxide evolution was required. Typical sets of results for three runs are shown in Tables B, C and D.

Table B. Reaction between Ethyl Cyanoacetate and Thionyl Chloride

Volume of Na2S203(cm3)	Weight of SO <sub>2</sub> (g)	Time (hours)
10.35	0.0394	1/3
10.10	0.0790	<u>-</u> 23
9.60	0.1566	1
9•45	0.1793	1호
9.05	0.2388	1중
8.45	0.3261	2
7.80	0.4185	21/3
7.20	0.5019	2중
6.65	0.5765	3
6.20	0.6362	313
5.85	0.6814	38
1.50	1.2297	8

Normality of iodine solution (I) = 0.107

Normality of Sodium thiosulphate solution (S) = 0.101

Table C. Reaction between Ethyl Cyanoacetate and Thionyl Chloride with

Tetrachloro-p-benzoquinone (5%)

Volume of $Na_2S_2O_3$ (cm <sup>3</sup> )	Weight of SO <sub>2</sub> (g)	Time (hours)
10.35	0.0394	13
10.00	0.0948	245
9.65	0.1491	1
9.20	0.2175	113
8.75	0.2844	1읗
8.15	0.3716	. 2
7.60	0.4499	23
6.90	0.5471	23
6.45	0.6082	3
6.20	0.6414	33
5.85	0.6866	33
1.60	1.2223	8

Normality of iodine solution (I) = 0.107

Normality of sodium thiosulphate solution (S) = 0.101

Table	• D.	Reaction	between	Ethyl	Cyanoacetate	and	Thionyl	Chloride
with	Diber	nzoyl Pero	xide(0.	1%)	Market Star	94. A		ANY ANY

Volume of Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub> (cm <sup>3</sup> )	Weight of SO <sub>2</sub> (g)	Time (hours)
a substantia and a substantia		
10.45	0.0232	1 <u>3</u>
10.00	0.0945	23
9.50	0.1721	1
9.10	0.2328	1큥
8.85	0.2700	1중
8.30	0.3500	2
7.65.	0.4424	2=3
7.30	0.4911	23
6.45	0.6064	3
6.05	0.6594	3=3
5.50	0.7306	3을
1.05	1.2915	8

Normality of iodine solution (I) = 0.107Normality of sodium thiosulphate solution (S) = 0.101

The reactions were allowed to continue for a further four hours after which time the reaction was stopped by pouring the mixture into chloroform (150 cm<sup>3</sup>). The solution was washed with water and sodium bicarbonate solution to remove the thionyl chloride, dried with anhydrous magnesium sulphate, and then the solvent was removed under reduced pressure. The product (diethyl dicyanofumarate) was recrystallised from the minimum quantity of ethanol (95%). The titration figures for the reactions after eight hours were also recorded and from these the percentage reaction was calculated from the equation below and compared with the figure from alkene value.

$$2CNCH_2CO_2Et + 2SOC1_2 \longrightarrow CN CO_2Et + 4HC1 + SO_2 + S$$
  
EtO\_2C CN + 4HC1 + SO\_2 + S

The weights of sulphur dioxide were reduced by 0.25 g (obtained by extrapolation of the results in Table A) to allow for sulphur dioxide from thionyl chloride. The results are as follows,

	Corrected weight of SO <sub>2</sub> (g)	% Yield	% Yield of Diethyl Dicyanofumarate
Table B	0.9797	65.3	61.2
Table C	0.9723	64.5	60.9
Table D	1.0415	69.4	65.1

All the experiments were repeated three times except the ethyl cyanoacetate/thionyl chloride blank which was run with each experiment. The main error in the experiment was from the titration figures which were at their worst at the beginning of the experiment. On average they were found to be  $\pm 0.25$  cm<sup>3</sup> in 10 cm<sup>3</sup>, i.e.  $\pm 2.5\%$ .

-12-

#### Hydrogen Chloride

The weight of hydrogen chloride gas evolved from the reaction was calculated from the potassium thiocyanate titration figures (Appendix II) after adding an appropriate correction for hydrogen chloride derived from thionyl chloride. A typical set of results are shown in Tables E and F.

Table E. Titration Results (Volume of Potassium Thiocyanate in cm<sup>2</sup>)

Reaction Mixture	Blank	10.20-Blank	Corrected Volume of KCNS
9.90	10.20	0	9.90
9.75	10.15	0.05	9.80
9.40	10.10	0.10	9.50
9.20	10.05	0.15	9.35
8.95	10.00	0.20	9.15
8.60	9.95	0.25	8.85
8.15	9.85	0.35	8.50
7.15	9.90	0.30	7.45
6.15	9.90	0.30	6.45
4.85	9.85	0.35	5.20

The value for the 'blank' is subtracted from 10.20, the value when no hydrogen chloride is present, and then added to the Reaction Mixture titre to give the Corrected Volume.

-13-

#### Table F. Calculated Results

Volume of KCNS(cm <sup>3</sup> )	Weight of HCl(g)	CNCH <sub>2</sub> CO <sub>2</sub> Et Remaining(moles)
9.90	0.0710	0.0449
9.80	0.0891	0.0445
9.50	0.1426	0.0430
9.35	0.1691	0.0423
9.15	0.2040	0.0413
8.85	0.2559	0.0399
8.50	0.3158	0.0372
7.45	0.4936	0.0334
6.45	0.6610	0.0288
5.20	0.8681	0.0231

Normality of Potassium Thiocyanate solution = 0.0499

Normality of Silver Nitrate solution = 0.1027

Volume of Silver Nitrate solution used = 5.0 cm<sup>3</sup>

The amount of ethyl cyanoacetate remaining after each titration was calculated from the equation,

 $CNCH_2CO_2Et + SOC1_2 \longrightarrow CNCHCO_2Et + HC1$ SoC1 a-x + a-x x + x

At the start of the reaction x=0 and a=0.0469 moles. From the figures in Table F, the results were plotted in the form shown in Table G.

Table G

Moles of CNCH <sub>2</sub> CO <sub>2</sub> Et (a-x)	1/(a-x)	$1/(a-x)^{\frac{1}{2}}$	Time (hours)
0.0469	21.32	4.617	0
0.0449	22.27	4.720	14
0.0445	22.47	4.742	1/2
0.0430	23.26	4.821	34
0.0423	23.64	4.861	- 1
0.0413	24.21	4.921	1쿺
0.0399	25.06	5.004	1출
0.0372	26.88	5.185	13
0.0334	29.94	5.474	2
0.0288	34.72	5.891	21/4
0.0231	43.27	6.579	21/2

The experiment was repeated three times. The concentration of the potassium thiocyanate solution had to be reduced to half that of the silver nitrate solution to reduce titration errors. The spread of the figures was then  $\pm 2.5\%$ .

3.3. The Reaction of Diethyl Malonate and a mixture of Disulphur Dichloride and Sulphuryl Chloride (p. 46)

The products of the reaction were analysed by g.l.c. using a Carbowax 20M column at 175°C. The following retention times were obtained and were identical to standard samples.

Compound	Retention Time (minutes)
Diethyl Malonate	1 <del>3</del>
Diethyl <-chloromalonate	3
Diethyl X,X-dichloromalonate	513
Tetraethoxycarbonylethene	approx. 14 (poor resolution)

-15-

### 3.8. Detection of Diethyl Dicyanomaleate (p. 52)

An infrared spectrum of the reaction mixture was found to have absorption bands at 2215 cm<sup>-1</sup> and 1630 cm<sup>-1</sup> which were attributed to diethyl dicyanomaleate (as described in the text). It was stated that the spot of  $R_f$  0.44 was probably diethyl dicyanomaleate. The assignment was based on the fact that the other two spots at  $R_f$  0.90 and  $R_f$  0.23 had been shown to be starting material (ethyl cyanoacetate) and diethyl dicyanofumarate respectively by running the known and unknown compounds alongside each other on the same plate. In a similar manner, the spot at  $R_f$  0.30 (1:1  $C_6H_6$ :CHCl<sub>3</sub>) was shown to be ethyl cyanoacetate by running an authentic sample alongside it. Since a sample of diethyl dicyanomaleate was not available, this procedure could not be used to detect the cis-isomer.

The mass spectrum of the two samples isolated by preparative t.l.c. ( $R_f$  0.44 and  $R_f$  0.23) showed that they were the same compound which could only be interpreted by the existence of two geometric isomers. Both samples showed a molecular ion peak at an m/e value of 222. Reference to the mass spectrum of diethyl dicyanofumarate (Fig. 1 and Table 5) will show the spectrum in detail, but a brief comparison is given below.

Diethyl Dicyanofumarate			
Known Compound	Compound from t.l.c.	Dietnyl Dicyanomaleate	
222 (1.7)	222 (1.1)	222 (2.1)	
193 (15)	193 (21)	193 (17)	
177 (100)	177 (100)	177 (100)	
150 (63)	150 (66)	150 (62)	
122 (40)	122 (39)	122 (40)	
105 (31)	105 (31)	105 (35)	
77 (95)	77 (97)	77 (91)	

Figures in brackets are relative intensities.

-16-

In addition to the peaks shown on the previous page, there were some fragments in both spectra that did not appear in the known sample of diethyl dicyanofumarate. Their relative intensities were in the order of 5-20 and occurred at 164 (maleate only), 255, 261, 279 and 326. These peaks are attributed to impurities, probably caused by streaking of a component of high  $R_f$  value. Thus the same extra component would appear in the spectrum of both alkenes.

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