STUDIES ON THIOXO- AND SELENOXO- MALONATES.

A Thesis presented in part fulfillment

of the requirement for the Degree of

Doctor of Philosophy

by

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University of Glasgow. © W. M. McGregor. October, 1989.

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ACKNOWLEDGEMENTS

DEDICATION

" ... in a time when RADIATION threatens de Earth

and bombs are built instead of homes,

when WAR replaces reason,

and for some strange reason we have no say in de matter,

I will have to dedicate dis book to all peace-loving people.

Dedicated to all peace-loving people, worldwide. "

- Benjamin Zephaniah.

QUOTATION

"I have often had cause to feel that my hands are cleverer than my head. That is a crude way of characterising the dialectics of experimentation. When it is going well, it is like a quiet conversation with Nature. One asks a question and gets an answer; then one asks the next question, and gets the next answer. An experiment is a device to make Nature speak intelligibly. After that one has only to listen."

– George Wald.

CONTENTS

ABSTRACT

Thermally labile cycloadducts of diethyl thioxomalonate (46) were found to be most easily synthesised, in reasonable yields, by heating the corresponding ketone (48) with phosphorus pentasulphide in pyridine. The cyclopentadiene adduct (93) and, more usefully, the anthracene adduct (95) were found to dissociate on heating to regenerate diethyl thioxomalonate which then reacted regiospecifically in situ with other dienes (retro-Diels-Alder reaction) or with (-)-β-pinene ('ene' reaction). These labile cycloadducts (93) and (95) were oxidised with peracid to the corresponding S-oxides (173) and (172). These S-oxides also dissociated on heating, to give diethyl thioxomalonate S-oxide (148) which reacted in situ, regioselectively, with other dienes. Flash vacuum pyrolysis of the anthracene adduct (172) also liberated (148), free of anthracene, which enabled studies on the 'isolated' species (148) at lower temperatures.

Less success was achieved in synthesising cycloadducts of diethyl selenoxomalonate (229). This species was generated in situ by treating either diethyl selenocyanatomalonate (244) or the selenosulphate (250) with triethylamine in the presence of a diene. However, only the cyclopentadiene adduct (230) and the 2,3-dimethyl--1,3-butadiene adduct (244) were succesfully synthesised, in poor to moderate yields with low reproducibility.

CHAPTER 1

"THE SYNTHESIS AND REACTIONS OF DIETHYL THIOXOMALONATE."

INTRODUCTION

STABILITY OF THIOCARBONYL GROUPS

Consideration of the recent reviews on thiocarbonyl compounds[1-9] indicates the relative rarity of true thioketones, or thiones. The difficulty in making such species lies in the instability of the (2p-3p) π-bond between the "small" oxygen 2p and the "large" sulphur 3p orbitals; this poor orbital overlap leads to a weak π-bond.
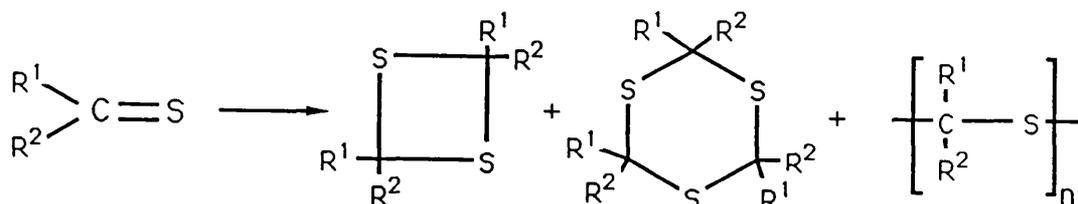
Scheme 1

Early attempts to isolate thioketone monomers produced, instead, oligomers or polymers of the thioketone (Scheme 1). The presence of an electron-donating group can stabilise the thiocarbonyl group by delocalisation and there are examples of stable thioamides[10](1), thionoesters[I] (2) and dithionoesters (3) and their corresponding acids[II].

(1)=NR^3
(2)=O
(3)=S
R^1,R^2,R^3=H,alkyl,aryl
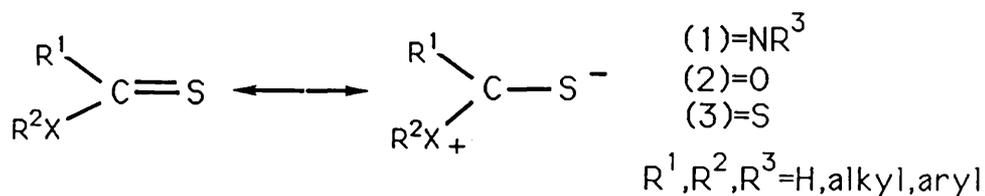
A good example of this kind of stabilisation was reported by Grishchuk in

1967 who produced the stable thioamide dithioester (4) shown in Scheme 2.[12]
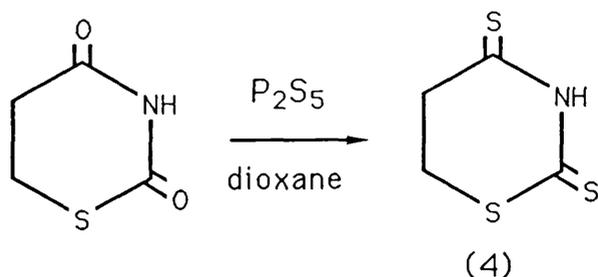
Scheme 2

In contrast, thiocarbonyl compounds with electron-withdrawing groups in

the α-position are even rarer in the chemical literature. The

electron-withdrawing group reduces the energy and size mismatch in the

(2p-3p) π-bond, thus destabilising further an inherently unstable

species. Some examples include those thiocarbonyl campounds with attached

ketonic[13](5), ester[14-17](6), and para-nitrophenyl[15](7) groups.

$$(5) \ Z=COR^2$$
$$(6) \ Z=CO_2R^2$$
$$(7) \ Z=p-NO_2C_6H_4$$
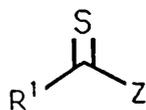
An alternative source of stability in thioketones is found when steric

congestion prevents rapid polymerisation, eg. both benzophenone[18](8) and

thiocamphor[19](9) are stable and blue (due to n-π* transitions).

(8)   (9)
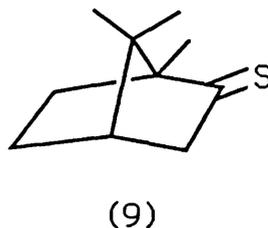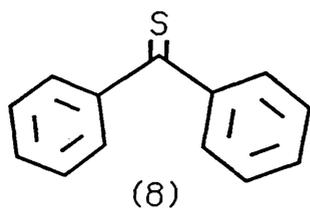
THE DISCOVERY AND SYNTHESIS OF THIOKETONES

The first report of a polymerised thioketone was by Hofmann[20], in 1868, who treated formaldehyde (10) with H_2S and HCl, and obtained the trimer (11) of thioformaldehyde[21] (12) as displayed in Scheme 3.
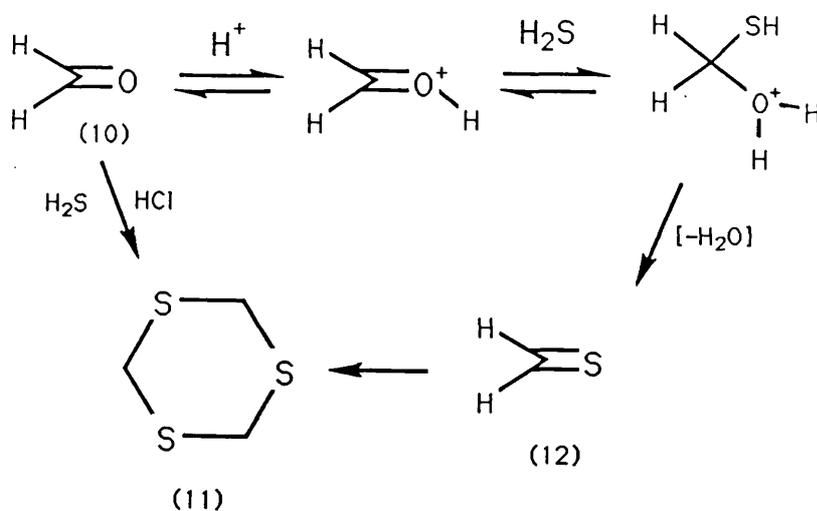
Scheme 3

Although H_2S and HCl have been used more recently[22] to generate thioketones, a wide range of other methods[23] has been developed for the synthesis of thioketones, perhaps the most successful being the use of phosphorus pentasulphide (in fact P_4S_{10}). This reagent was first used[23,24], in 1886, on the ketone (13) to generate Michler's thione (14) in good yield

(Scheme 4). The thione (14) is stable because of the delocalisation of the

nitrogen lone pairs onto the sulphur atom via the conjugated ring system,

and also because of steric hindrance of polymerisation by the bulky

aromatic groups.
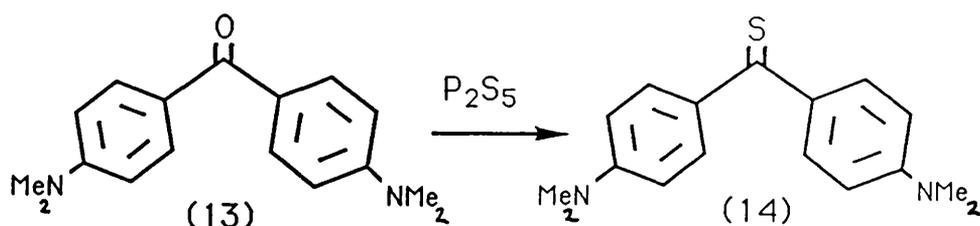
Scheme 4

The utility of phosphorus pentasulphide as a thionating agent has been

studied extensively in the synthesis of stable thioamides (1). The best

results appear to be achieved by using pyridine or diglyme as the solvent[25]

as phosphorus pentasulphide is appreciably soluble in both. However, in

other solvents where the P_2S_5 is present as a solid phase, the essentially

heterogeneous reaction can achieve successful results, especially if the

reaction is accelerated by the application of ultrasound[26].

Alternatively, addition of sodium bicarbonate to phosphorus pentasulphide, in pyridine or diglyme, liberates the proposed active species, S_2PS^-, (Scheme 5) which thionates amides in good yields[27].

$$2NaHCO_3 \ + \ P_2S_5 \ \longrightarrow \ NaS_2PS \ + \ NaOPS_2 \ + \ 2CO_2 \ + \ H_2O$$
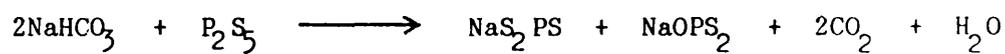
Scheme 5

GENERATION OF THIOCARBONYL COMPOUNDS BY RETRO DIELS-ALDER REACTION.

The earliest generation of a thioaldehyde by the retro-Diels-Alder

reaction was achieved by Baldwin and Lopez[28] in 1983. They generated

thiobenzaldehyde (20) by thermolysis of the thiosulphinate (18) and

trapped it in situ with anthracene in high yield (Scheme 6). This

anthracene adduct (22) on heating liberated thiobenzaldehyde (20) which

was trapped with 2,3-dimethyl-1,3-butadiene quantitatively to give (25).

They also formed thioacetaldehyde (21) from the thiosulphinate (19) and

trapped it in situ in high yields with both anthracene to give (23), and

with 9,10-dimethyl anthracene to give (24). As shown in Scheme 6, only

the 9,10-dimethyl anthracene adduct (24) dissociated on heating to give

thioacetamide (21) which was trapped in situ with

2,3-dimethyl-1,3-butadiene to give (26) quantitatively.

(18) R=Ph
(19) R=Et

(20) R=Ph
(21) R=Et

(22) R=Ph; R^1=H
(23) R=Et; R^1=H
(24) R=Et; R^1=Me

(22)

(25)

(24)

(26)
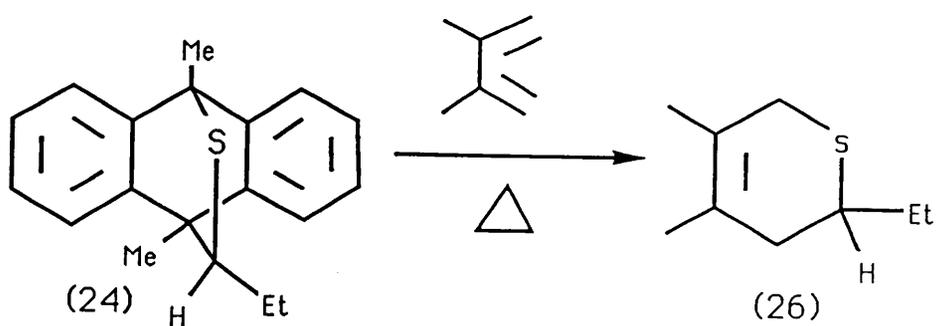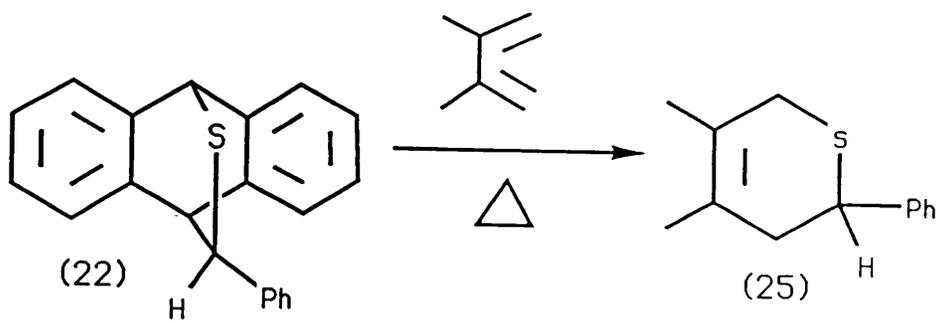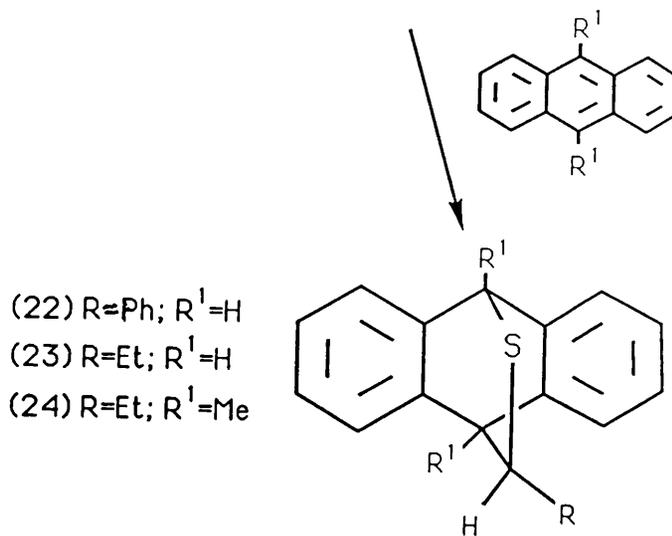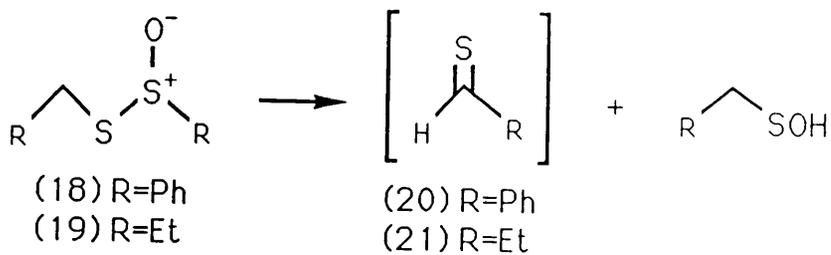
Scheme 6

It was later demonstrated by Kirby et al [15,16] (Scheme 7) that the

anthracene adduct (27) dissociated reversibly on heating to liberate ethyl

thioxoacetate (28) which was then trapped _in situ_ with

2,3-dimethyl-1,3-butadiene to give (29) quantitatively. Similarly, the

cyclopentadiene adducts (30) of a variety of thioaldehydes [16] dissociated

on heating to liberate the thioaldehydes (31) which were again trapped

with 2,3-dimethyl-1,3-butadiene to give (32).
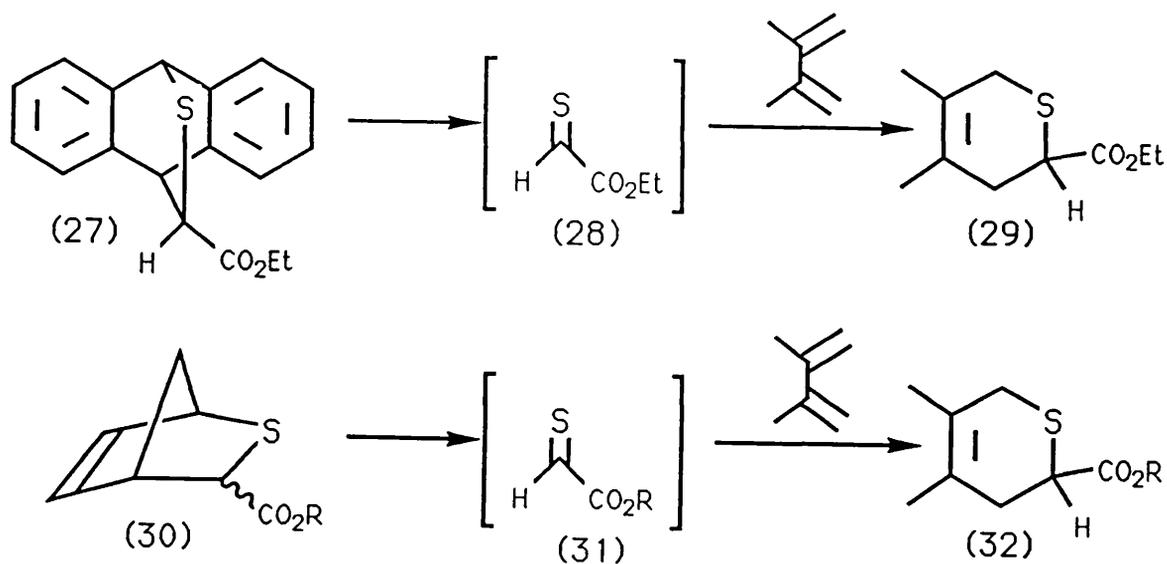
R=CO$_2$Et
  CONHPh
  COPh
  CN
  p- NO$_2$C$_6$H$_4$

Scheme 7

α-OXO THIOCARBONYL COMPOUNDS.

Amongst the thiocarbonyl compounds so far synthesised,

α-oxo-thiocarbonyl derivatives are rather uncommon. It was not until 1975

that Hohne synthesised such a species[13] by treating the dibromo compound

(33) with potassium O-ethyl xanthate (Scheme 8) to give an unstable

α-oxo-thioketone (34) which could be trapped in situ with

2,3-dimethyl-1,3-butadiene to give the heterocycle (35) by Diels-Alder

[4+2] cycloaddition.
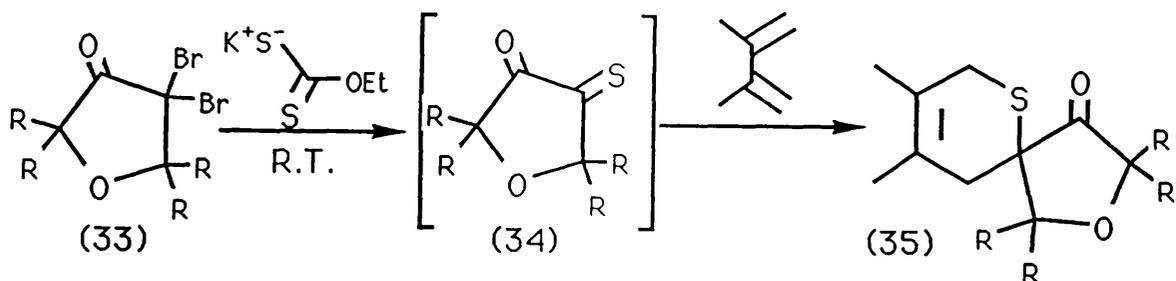
Scheme 8

Some thioaldehydes with α-ester groups have also been synthesised.[14-17]

One of the better synthetic routes involved base-catalysed elimination of

a phthalimido derivative of a mercaptoacetate[15] (36) to generate the

unstable thioaldehyde (28) which was again trapped in situ with a

conjugated diene, such as 2,3-dimethyl-1,3-butadiene to give (29) or with

anthracene to give (27) as illustrated in Scheme 7. When (28) formed in

this manner was trapped with cyclopentadiene a 7:3 mixture of the endo

adduct (37) and the exo adduct (38) was produced.

An alternative and "cleaner" way to generate (28) under neutral

conditions[15] is by heating either the anthracene adduct (27) or the

cyclopentadiene adducts (37) and (38), all of which underwent

retro-Diels-Alder reaction to liberate (28), which was then transferred

quantitatively to another conjugated diene (Schemes 7 and 9).
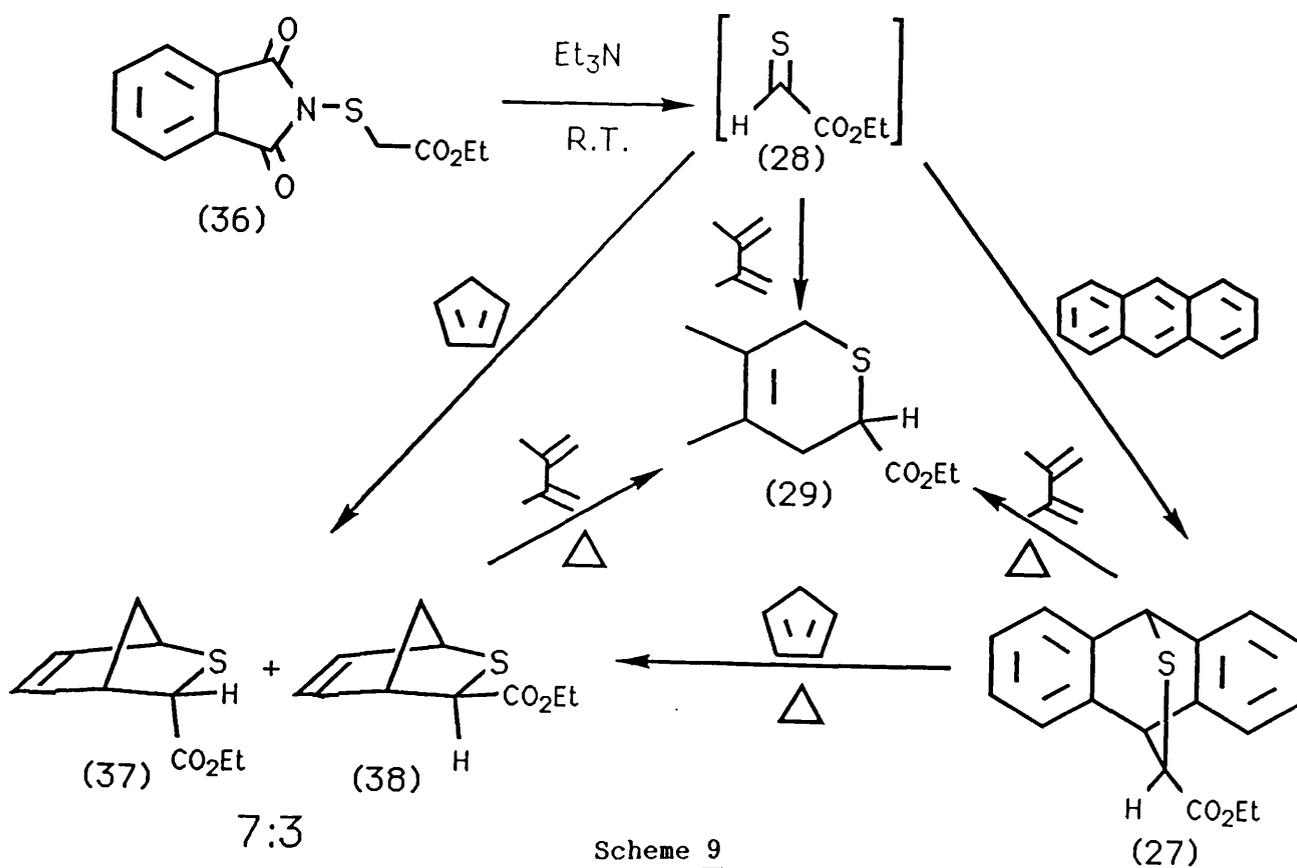
Scheme 9

The cycloaddition of (28), formed in this case from the sulphenyl chloride (39), to thebaine (40) gave as the major product[16] (41) under kinetic control (Scheme 10). This has the regioselectivity correctly predicted by simple frontier molecular orbital theory. However, on heating in refluxing toluene (41) dissociated then reassociated, eventually giving the thermodynamically more stable isomer (42).
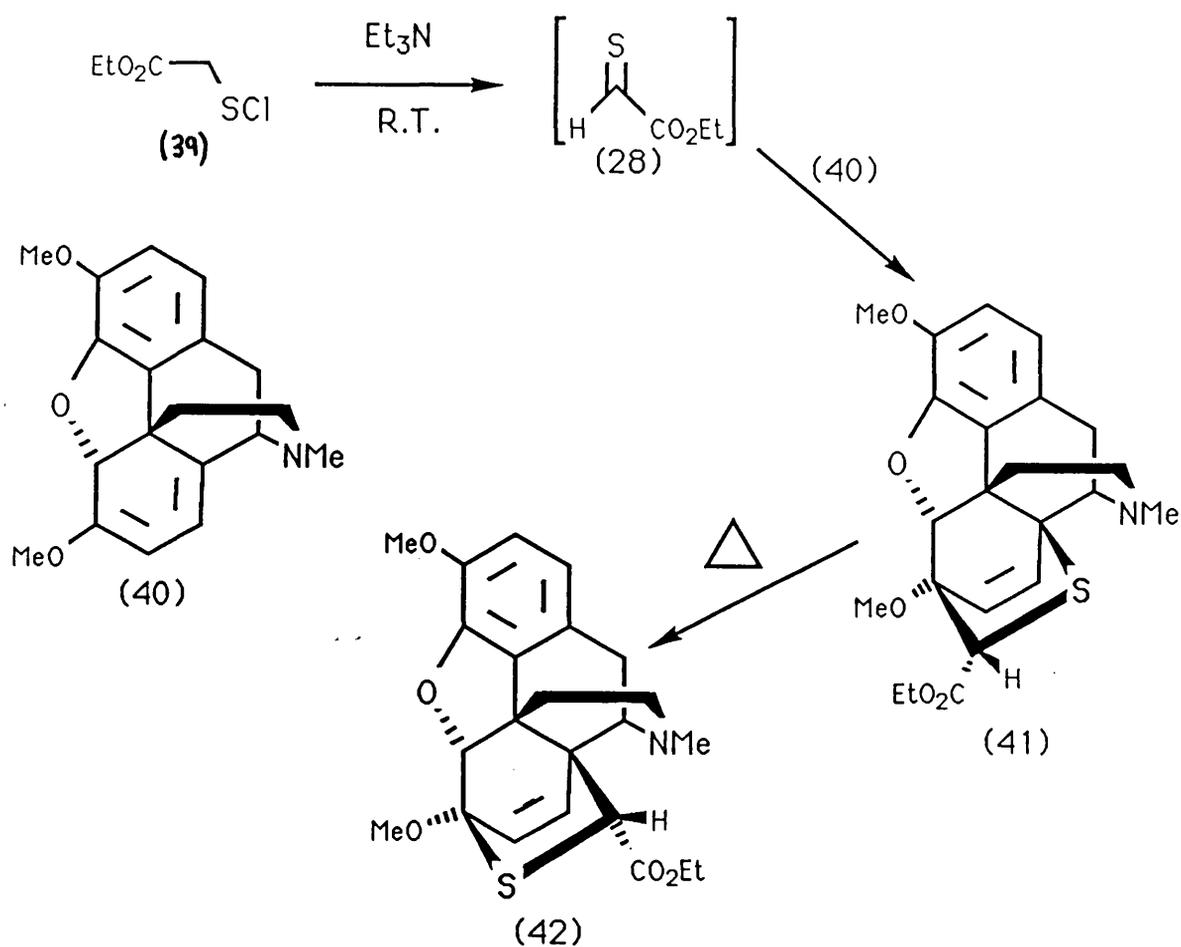
Scheme 10

Another convenient route to the thioester (28) involves heating a

triphenyl phosphonium ylid (43) with elemental sulphur[17] (Scheme 11). The

intermediate thioaldehyde apparently underwent in situ nucleophilic attack

at carbon by morpholine to give the stable thioamide (44). The

thioxoester (28) produced in this manner has, however, not been trapped in

any other way.
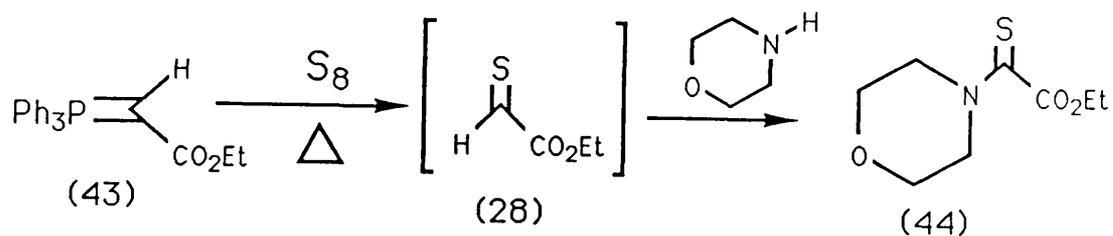
Scheme 11

THIOXOMALONATE ESTERS.

Very little work has been published on thioxomalonates, the thioketones related to oxomalonate esters. Their rarity is, of course, due to the considerable destabilising influence of having two electron-withdrawing groups attached to the thiocarbonyl group which makes thioxomalonates very highly reactive. Hence, it was not until 1978 that diethyl thioxomalonate (46) was first synthesised by Beelitz et al[29] who treated the dibromomalonate (45) with potassium O-ethyl xanthate (Scheme 12) to give (46) which then reacted in situ with 2,3-dimethyl-1,3-butadiene to give the cycloadduct (47) in 70% yield.
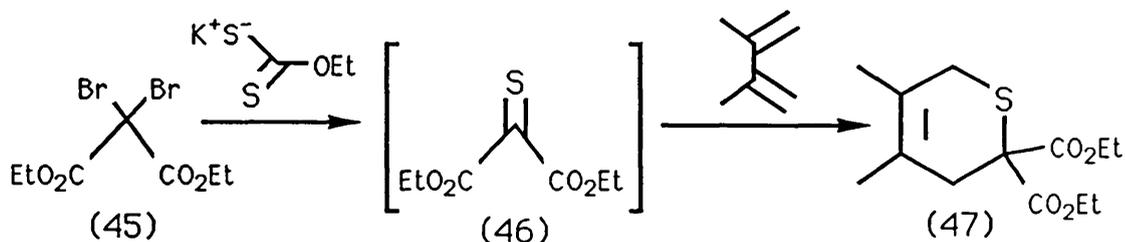
Scheme 12

Diethyl thioxomalonate (46) also featured in the, as yet, incomplete

synthetic route[30] to thiathromboxanes (51) displayed in Scheme 13.

Generation of (46) from diethyl oxomalonate (48) with P_2S_5 and subsequent

hydrolysis, with spontaneous decarboxylation, of the adduct (49) gave the

diacid (50).

Scheme 13
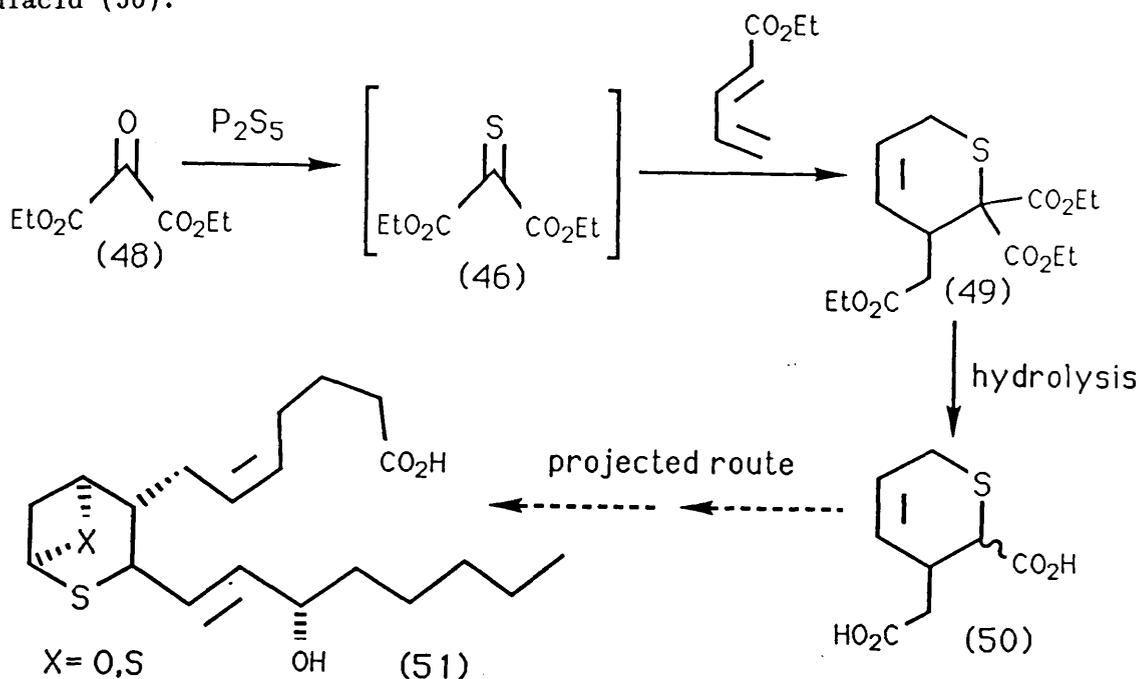
REACTIONS OF THE THIOCARBONYL GROUP

Most of the studies on thiocarbonyl reactivity have been conducted, for convenience, on stable thiocarbonyl compounds[31]. These studies have shown that thiocarbonyl chemistry is, in general, analogous to that of the corresponding carbonyl compounds, except that the inherent instability of the C-S π-bond increases rates of reaction. For example, thiobenzophenone (8) reacts with phenylhydrazine (Scheme 14) 2000 times faster[32] than benzophenone (52), to give the same hydrazone product (53).

(8) X=S
(52) X=O

(53)
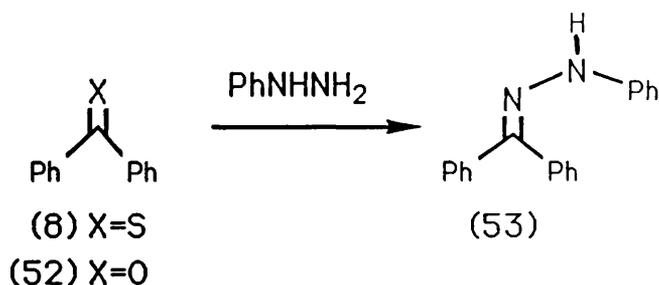
Scheme 14

Similarly, reduction of thioketones (54) to thiols (56) with sodium borohydride (Scheme 15) proceeds much faster[1,32] than the corresponding reduction of carbonyls (55) to alcohols (57).

$$R^1 \overset{X}{\underset{}{\diagup\!\!\diagdown}} R^2 \quad \xrightarrow{\text{NaBH}_4} \quad \overset{H\diagdown \diagup XH}{R^1 \diagup \diagdown R^2}$$

(54) X=S   (56) X=S

(55) X=O   (57) X=O
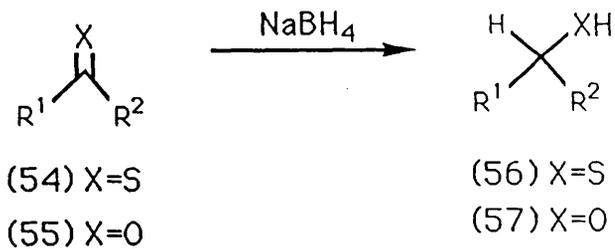
Scheme 15

Marked differences in chemistry are, however, observed between the reactions of thiocarbonyl and carbonyl groups in the following cases: oxidation (which gives sulphines from thiocarbonyl compounds – see Chapter 2), reactions involving nucleophiles, and reactions with dienes or mono-olefins.

(a)   REACTIONS OF THIOCARBONYL GROUPS WITH NUCLEOPHILES.

With carbonyl compounds most nucleophilic reactions occur with attack at the carbonyl carbon. Analogous reactions involving thioketones[1,2] include the formation (Scheme 16) of acetals (58) and thioacetals (59).
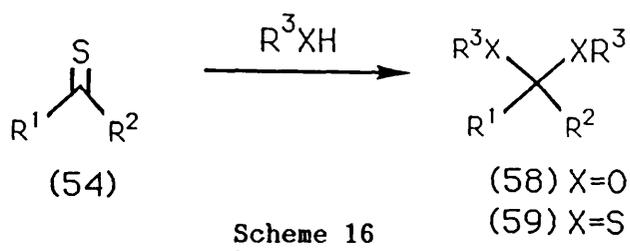
Scheme 16

However, contrasting nucleophilic attack at sulphur (Scheme 17) can occur on treatment of thioketones with phenyl-lithium[1,2] to give thioethers (60) , and with sodium bisulphite to give thiosulphates (61).

Scheme 17
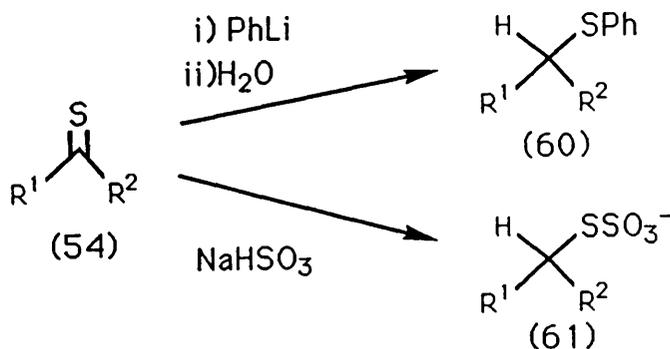
(b)   REACTIONS OF THIOCARBONYL GROUPS WITH CONJUGATED DIENES.

Although carbonyl compounds can undergo Diels-Alder cycloadditions, thiocarbonyl compounds react much faster[33] and in many cases where the corresponding carbonyl compound is unreactive, the thioketone will be reactive towards conjugated dienes. For example, in Scheme 18, hexafluoro~~ac~~etone (62) reacts with 1,3-butadiene at -78°C to give the heterocycle (63) by Diels-alder cycloaddition, whereas hexafluoroacetone (64) has to be heated with a more reactive diene in order to obtain the product (65).
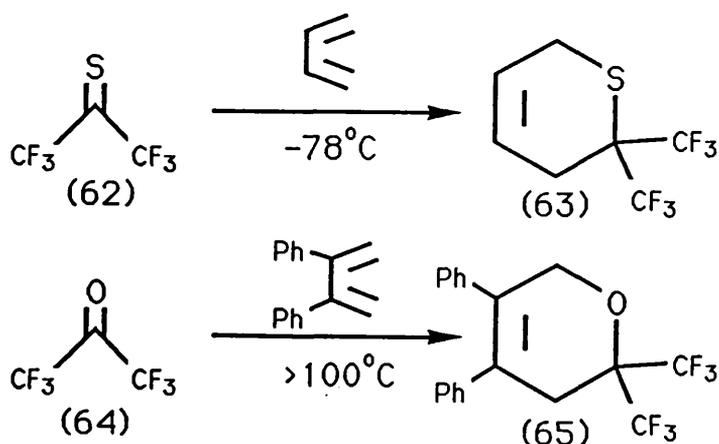
Scheme 18

Thus the high reactivity of thioketones (and thiocarbonyl compounds in general) towards conjugated dienes provides a useful method of "trapping" unstable thioketones produced in situ before they polymerise [9].

Regiochemistry of Diels-Alder Reactions.

Frontier molecular orbital theories predict that the regioselectivity[34] of cycloaddition reactions involving thioketones with electron-withdrawing groups (Z) should be as shown in Scheme 19, with the adduct (66) as the major product. The presence of electron-donating groups (X) on the diene will accelerate the reaction.

X= electron-donating group
Z=electron-withdrawing group Scheme 19
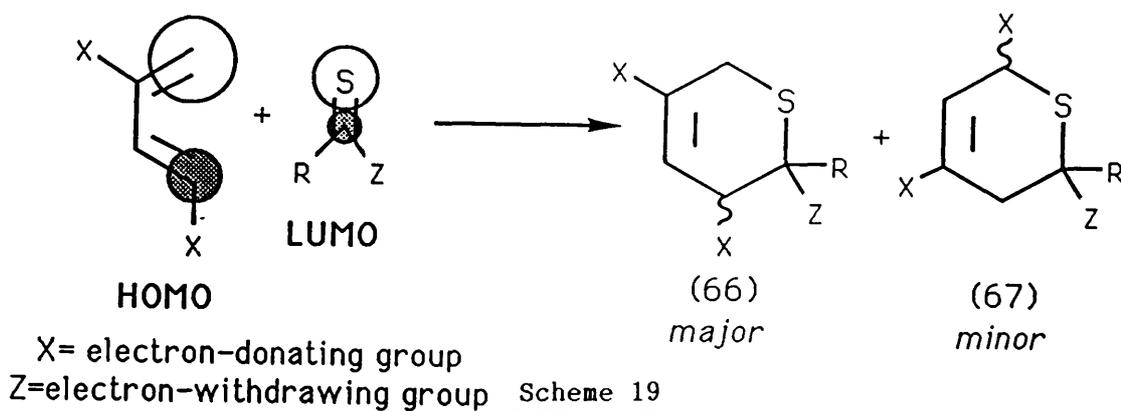
An early example of this kind of regioselectivity was observed in the reaction of the dithioester (68) with 1-methoxy-1,3-butadiene (Scheme 20) to give a 4:1 mixture of the regioisomers (69) and (70).[35]
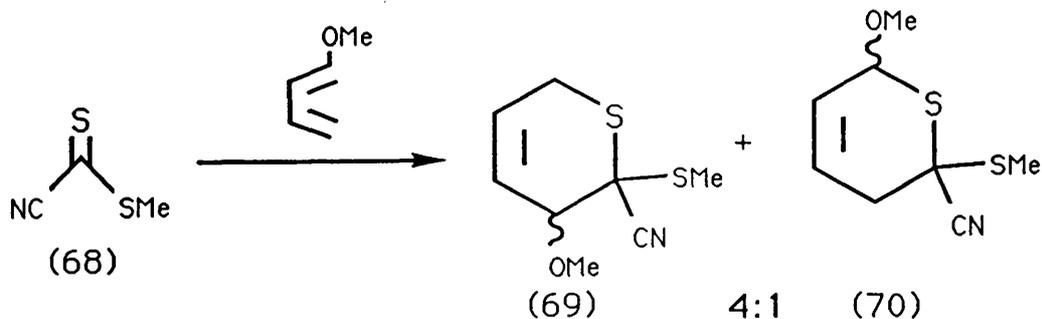
Scheme 20

Vedejs and coworkers[28,34,36] showed, more comprehensively (Scheme 21), that the presence of an electron-withdrawing group will promote the regiochemistry predicted in Scheme 19. They showed that addition **in situ** of (71) to (72) will produce (73) by Path A as the **major product.** Conversely, when the thioaldehyde (72) has no electron-withdrawing group, the inverse regioselectivity was observed by Path B to give mainly (74).
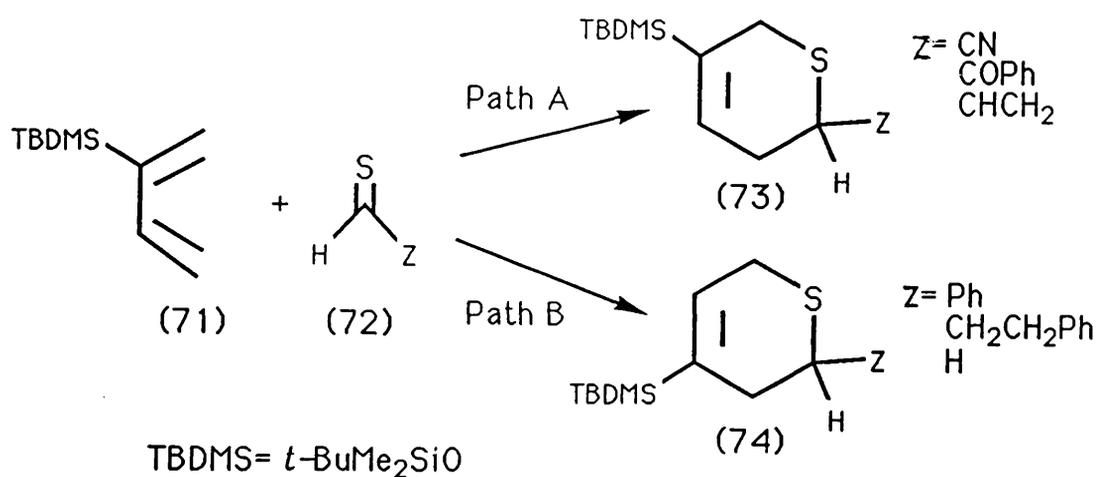
Scheme 21

(c)   REACTIONS OF THIOCARBONYL COMPOUNDS WITH MONO-OLEFINS.

Thiocarbonyl compounds can also undergo 'ene' reactions with suitable olefins. The dithionoester (68) was shown by Snider[37] in 1976 to undergo such a reaction (Scheme 22) with various olefins (75), exclusively with C-S bond formation (to give a thioacetal (77) and no thiol). In those cases where $R^2=R^4=H$, the product was formed predominately with a <u>trans</u> double bond, as can be predicted from the conformation of the transition state (76). Experiments with highly substituted or endocyclic alkenes (e.g. cyclohexene) gave little or no 'ene' product.
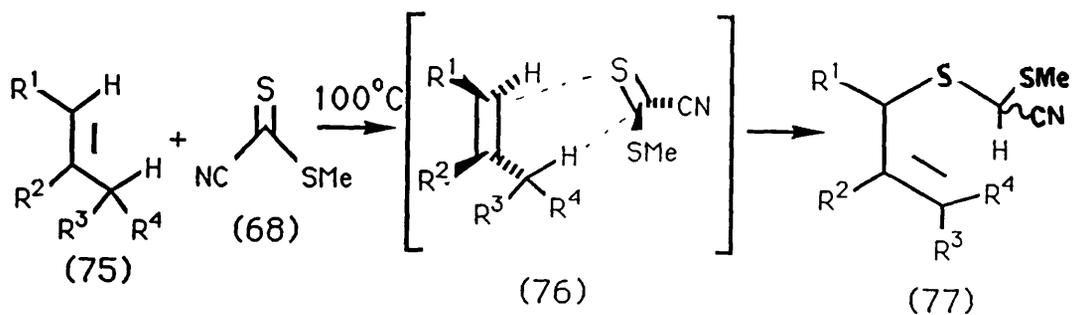
Scheme 22

Baldwin and Lopez[28] formed thiobenzaldehyde (20), by the method in
Scheme 6, which underwent an 'ene' reaction (Scheme 23) with (-)-β-pinene
(78) give a 1:2 mixture of (79) and (80) in moderate yield. This
preference for C-C bond formation is analogous to that observed for
carbonyl compounds[38] .
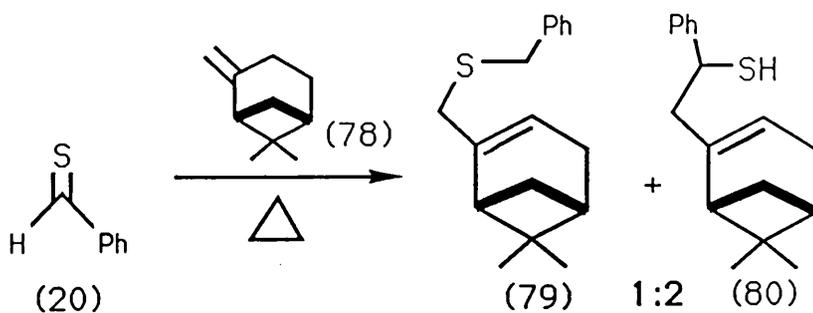
Scheme 23

Similarly, ethyl thioxoacetate (28), formed by retro-Diels-Alder cleavage
of the anthracene adduct (27), as in Scheme 7, underwent an 'ene' type[16,36]
reaction (Scheme 24) <u>in situ</u> with (-)-β-pinene (78) to give the products
(81) with C-S bond formation, and (82) with C-C bond formation, in a 4:1
ratio.
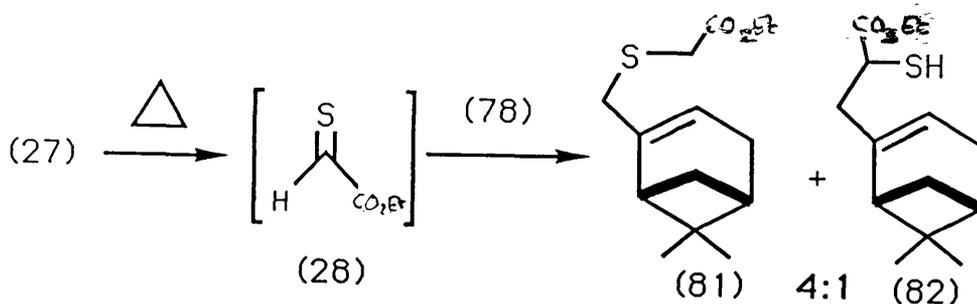
Scheme 24

This compares with the 1:2 ratio observed in Scheme 22, and demonstrates
that the presence of an electron-withdrawing group enhances the reactivity
of the thioaldehyde, and increases the regiochemical preference for C-S
bond formation.

The preference for C-S bond formation in the 'ene' reactions of thioxoacetates can, however, be reversed in intramolecular reactions. Thus (83) cyclised preferentially[39] with C-C bond formation (Scheme 25) to give the thiol (84) purely for conformational reasons.
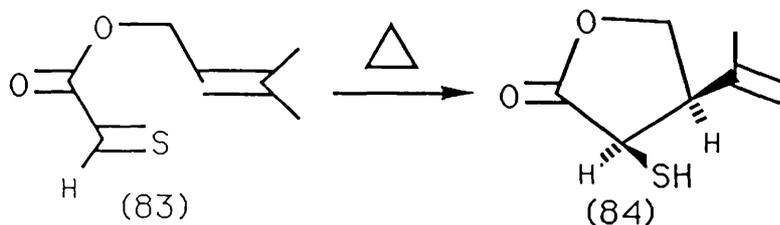
Scheme 25

Similarly the thioaldehyde (85), on heating, gave exclusively (Scheme 26) the thiol (86) in good yield[36], again demonstrating a preference for C-C bond formation because of conformational constraints.
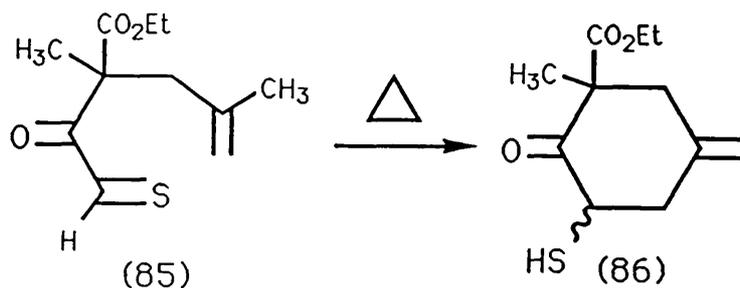
Scheme 26

DISCUSSION

SYNTHESIS OF DIETHYL THIOXOMALONATE (46)

Diethyl thioxomalonate (46) is of potential synthetic utility because of the flexibility of the malonate moiety. Once the thione (46) has been synthetically incorporated into a structure (87), the two ester groups provide convenient sites for further synthetic manipulation (Scheme 27), e.g. hydrolysis and decarboxylation to give a monoacid (88), which could be esterified to (89) or reduced to the alcohol (90). The acid (88) should be readily susceptible to electrophilic attack at the α -position via the corresponding carbanion.
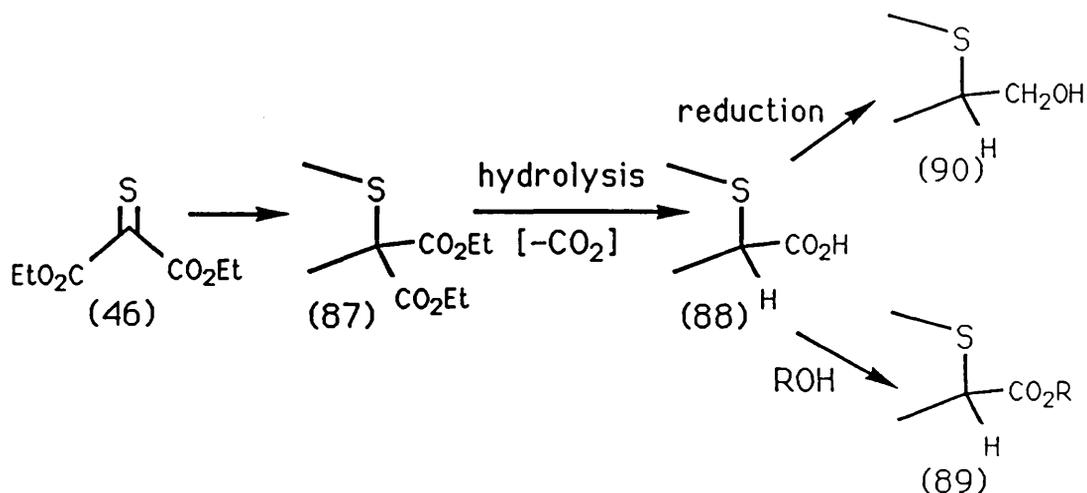
Scheme 27

It was already known[40] (Scheme 28) that diethyl 2-bromomalonate (91)

reacted with sodium thiosulphate to give the thiosulphate salt ester, or

"Bunte" salt, (92). This salt (92), on treatment with triethylamine, gave

the thione (46) which was trapped _in situ_ with cyclopentadiene to give the

cycloadduct (93). Some decarboxylated product (30) was also obtained. It

is unlikely that this method could be extended to trap (46) _in situ_ with

anthracene: generally "Bunte" salts need to be used with reactive dienes

such as cyclopentadiene.
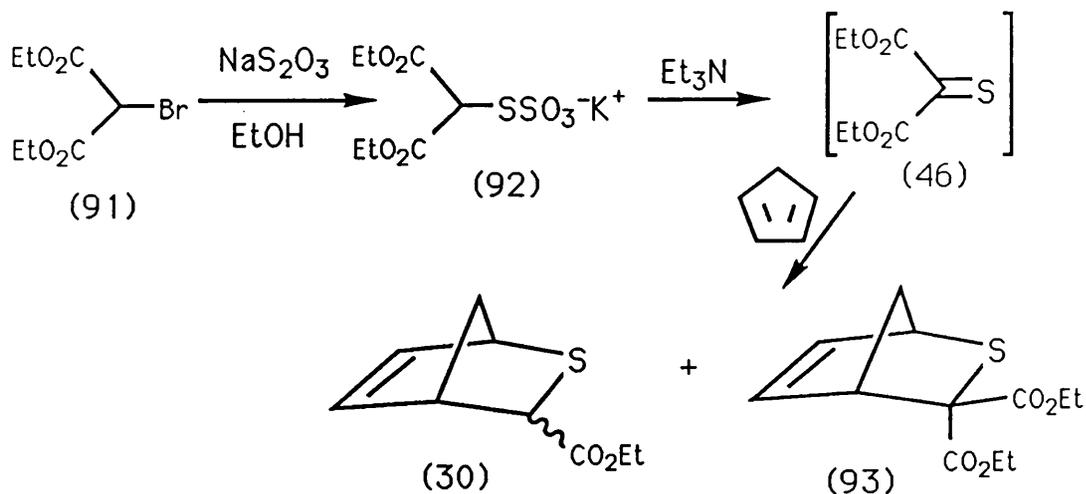
Scheme 28

A literature preparation [29] of diethyl thioxomalonate (46) involves
(Schemes 12 and 29) treatment of diethyl 2,2-dibromomalonate (45) with two
molar equivalents of O-ethyl xanthate [4I] (94). The diester (45) is most
conveniently prepared by reacting two moles of bromine with diethyl
malonate in carbon tetrachloride under strong light [42]. The thione (46)
generated in situ by this method was trapped by 2,3-dimethyl-1,3-butadiene
(15 mol. equiv.) at 0°C in acetone to give the cycloadduct (47) in 70%
yield.
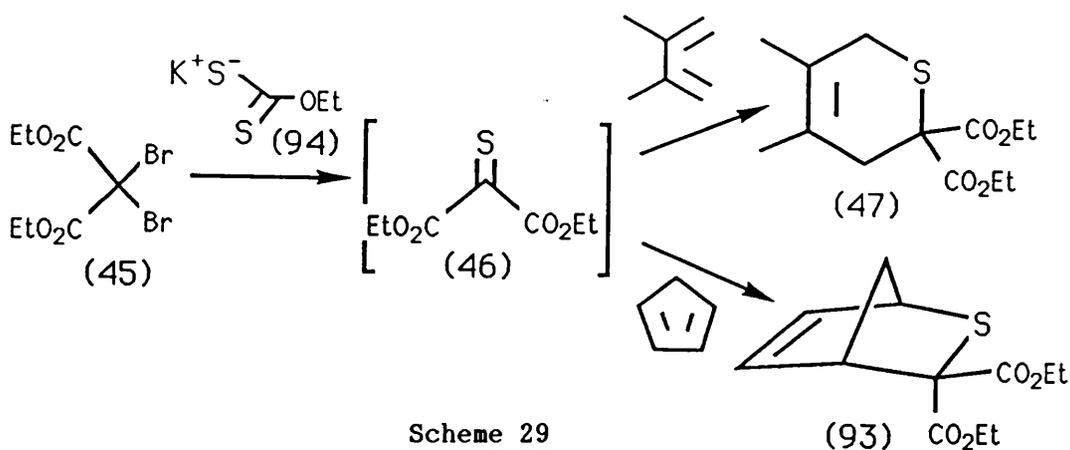
Scheme 29

This procedure was successfully repeated and extended (Scheme 29) to
include trapping the thione (46) at 0°C with cyclopentadiene (15 mol.
equiv.) to give (93) in 59% yield. However, with anthracene as the
"trapping diene" no cycloaddition product was observed, even when the
reaction was carried out under reflux for 1h. Presumably, anthracene is
insufficiently reactive to trap the thioketone (46) in the presence of
nucleophiles, such as the xanthate (94).

It had also been shown[43] that diethyl oxomalonate (48), which is commercially available, will react with phosphorus pentasulphide (in fact, P_4S_{10}) in refluxing benzene overnight (Scheme 30) in the presence of anthracene to give (95) in low yield (5-10%). Presumably, the thioketone (46) is again an intermediate. Hydrolysis of the diester (95) with aqueous sodium hydroxide gave, with spontaneous decarboxylation, the corresponding monoacid (96).
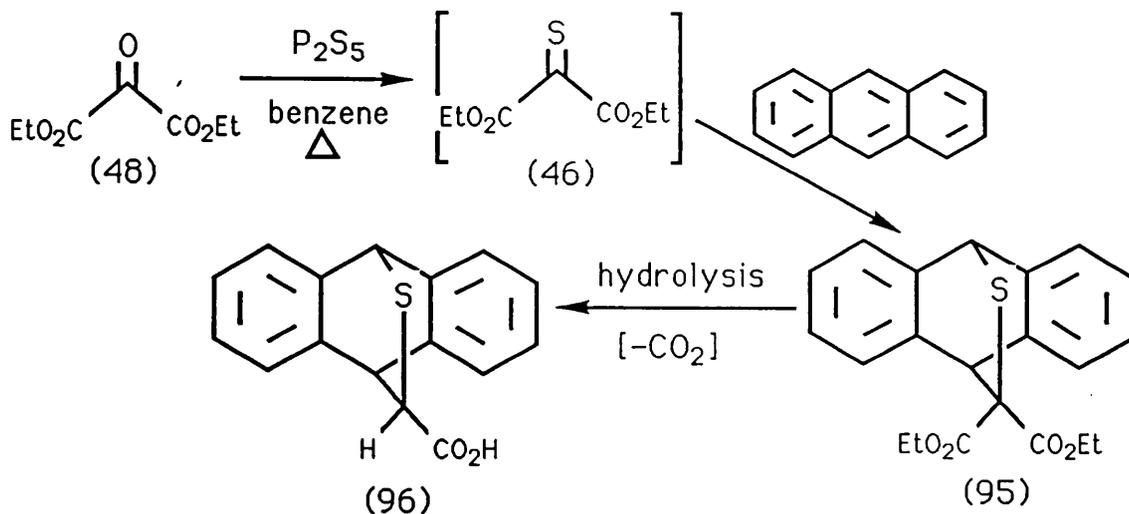
Scheme 30

Ater considering the methods already known for the synthesis of the thioxomalonate (46), and particularly since we required the anthracene adduct (95), we needed an improved synthesis of (95), especially with an increase in yield. Potential difficulties in improving the reaction in Scheme 30 included the sensitivity of both the starting ketone (48), and especially of phosphorus pentasulphide, to moisture, necessitating the use of carefully dried solvents. A potentially greater problem was the insolubility of the reagent in most organic solvents: for example, the reaction was essentially heterogeneous in refluxing benzene.

Various approaches, described as follows, were tried in order to improve the synthesis of the anthracene adduct (95).

(a)   ULTRASONIC IRRADIATION.

It is well documented that, in certain cases, ultrasonic irradiation can accelerate heterogeneous reactions[44]. A relevant case was reported by Raucher and Klein[26], who showed that the rates of reaction of phosphorus pentasulphide in tetrahydrofuran (THF) at room temperature, with a variety of amides, was substantially increased, giving the corresponding thioamides in high yields.

However, when a suspension of phosphorus pentasulphide (0.2 mol. equiv. -i.e. 1 equiv. of S atoms) and anthracene (3 mol. equiv.) in dry benzene containing diethyl oxomalonate (48) was irradiated at room temperature for 6h in a Mettler Electronics ME1.5 Ultrasonic Cleaning Bath, only a low yield (5-10% determined spectroscopically) of the desired anthracene adduct (95) was obtained. Similarly, experiments using dry THF or dry benzene/THF gave only low yields of (95) under these conditions.

(b)   USING P_2S_5/NaHCO$_3$.

It was known that the thionation of uracils could be improved by the
addition of sodium bicarbonate to a solution of phosphorus pentasulphide
in hot diglyme[27] (phosphorus pentasulphide is reasonably soluble in
diglyme). This liberates the proposed active species, S_2PS^- (Scheme 5).
Emulating this method, sodium bicarbonate (1 mol. equiv.) was added
(sufficiently slowly to control effervescence) to a stirred solution of
phosphorus pentasulphide (0.2 mol. equiv.) and diethyl oxomalonate (48)
(1 mol. equiv.) and cyclopentadiene (5 mol. equiv.) in diglyme at
ca.100°C. (Because of the low yields obtained so far with anthracene, it
became more convenient to use cyclopentadiene as a "trapping agent" to
investigate these reactions.) Heating was continued for 24h. This
experiment gave only a low yield (20-30% determined spectroscopically) of
the cyclopentadiene adduct (93). This yield was too discouraging to merit
investigation into the use of these conditions in making the anthracene
adduct (95).

(c)   USING P_2S_5 IN PYRIDINE.

Several thionation reactions have been successfully performed in a

solution of phoshorus pentasulphide in pyridine[25]. We have found that

this homogeneous reagent is very useful in the synthesis of diethyl

thioxomalonate (46).

Cyclopentadiene or 2,3-dimethyl-1,3-butadiene (5 mol. equiv.) and

phosphorus pentasulphide (0.4 mol. equiv. -i.e. 2 equiv. of S atoms) were

dissolved in refluxing dry pyridine, and diethyl oxomalonate (48) (1 mol.

equiv.) was added. After a further 1h heating the corresponding

Diels-Alder cycloadducts, (93) and (47), of diethyl thioxomalonate (46)

were isolated, both in yields of ca.60% (Scheme 31).

Refluxing pyridine is apparently too hot for the synthesis of the

anthracene adduct (95), since no (95) was isolated from the foregoing

conditions with anthracene replacing the other dienes. However, when

diethyl oxomalonate (48) (1 mol. equiv.) was added to anthracene (3 mol.

equiv.) and phosphorus pentasulphide (0.4 mol. equiv.) in dry pyridine at

70-80°C and heated for a further 1h, the desired anthracene cycloadduct

(95) was obtained (Scheme 31) in improved yield (25-30% ex MeOH). This

lower yield is a reflection of the poorer reactivity of anthracene[45] as a

dieneophile, when compared to cyclopentadiene or 2,3-dimethyl-1,3-

-butadiene.   This is in accordance with the observation that (95) does not

decompose when heated alone at 80°C in pyridine and that, therefore, the

lower yield is not due to decomposition of the product (95).

Yields of all three adducts (47), (93), and (95) are, however,

substantially reduced if the pyridine is not carefully dried before use,

largely because of the sensitivity of phosphorus pentasulphide to

moisture.

EtO₂C   CO₂Et
(95)

P₂S₅/py   70-80°C
C₁₄H₁₀

111°C

111°C

EtO₂C   CO₂Et
(48)

P₂S₅/py
C₆H₁₀   115°C

P₂S₅/py
115°C   C₅H₆

CO₂Et
CO₂Et
(47)

CO₂Et
CO₂Et
(93)

111°C
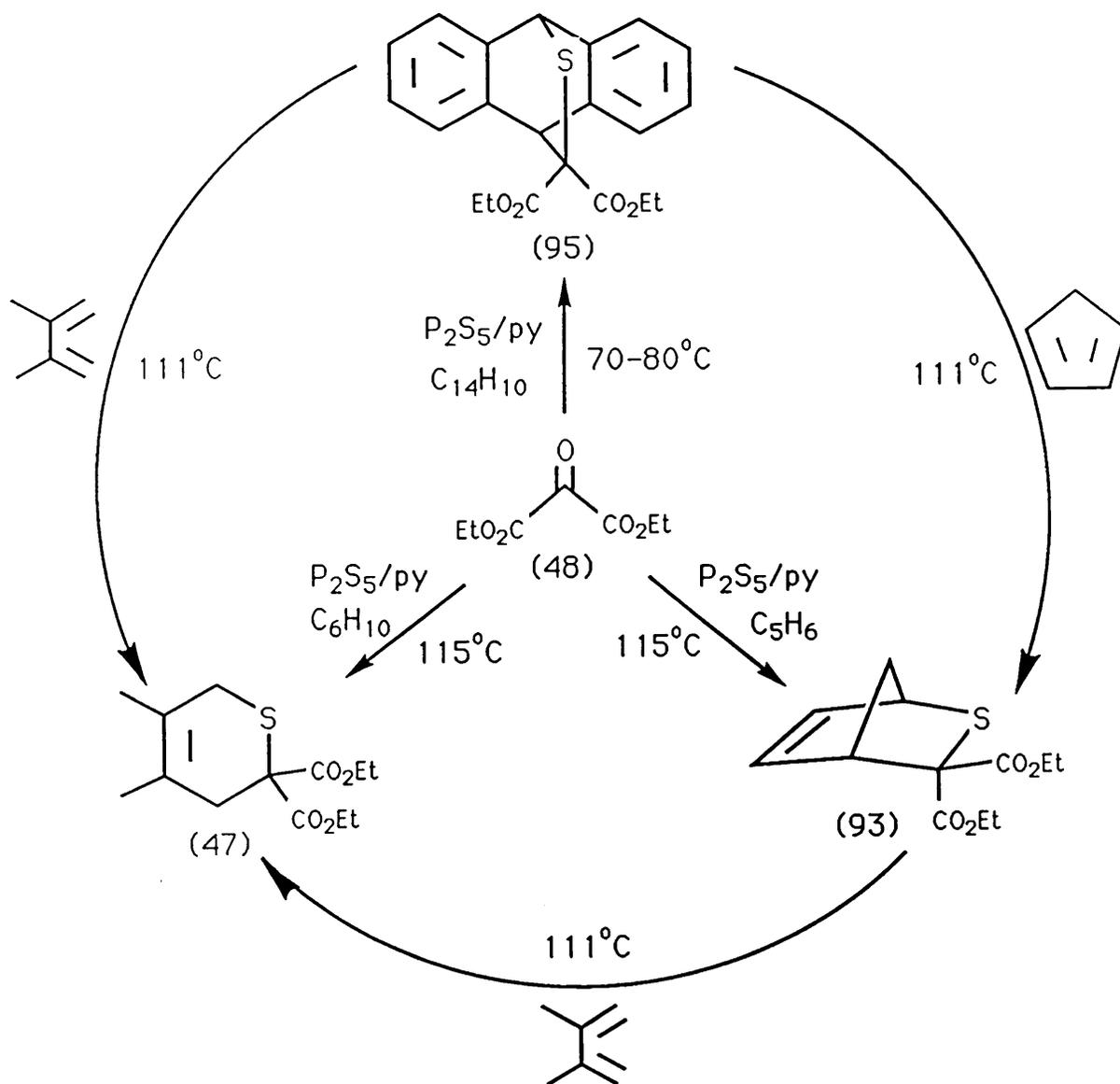
Scheme 31

REGENERATION OF DIETHYL THIOXOMALONATE (46) BY RETRO-DIELS-ALDER REACTION

The anthracene and cyclopentadiene adducts, (95) and (93), of the thione (46) are thermally labile and act as convenient "clean" precursors to the thione (46) on heating. As will be described, the rate of dissociation of the anthracene adduct (95) is faster than that of the cyclopentadiene adduct (93). This, in conjunction with the convenience of working with a crystalline adduct, makes the anthracene adduct (95) the preferred precursor to diethyl thioxomalonate (46).

Both the anthracene adduct (95) and the cyclopentadiene adduct (93) dissociate and recombine on heating. When there are no other reactants present, the cycloadducts are regenerated. Thus after 24h in refluxing toluene the cyclopentadiene adduct was recovered quantitatively, and the anthracene adduct recovered in good yield (75%).

The anthracene adduct (95) dissociated in refluxing toluene (Scheme 31) to liberate the thione (46), which was trapped in situ, over 1h, by either cyclopentadiene or 2,3-dimethyl-1,3-butadiene (5 mol. equiv.) to give the adducts (93) or (47), quantitatively. Similarly, the cyclopentadiene adduct (93) dissociated in refluxing toluene (Scheme 31) to give the thione (46) which was trapped in situ, over 1h, by 2,3-dimethyl-1,3--butadiene (5 mol. equiv.) to give the adduct (47) quantitatively.

(a)   COMPETITION EXPERIMENT.

Cyclopentadiene undergoes a Diels-Alder reaction with maleic anhydride, at 30°C, ca.275 times faster[45] than does 2,3-dimethyl-1,3-butadiene. Thus, it would be expected that in a competition experiment between these two dienes for such a dieneophile, the only isolated product would be the cyclopentadiene adduct. However, we were interested to see if this would still be the case using diethyl thioxomalonate (46) as the dieneophile.

To this end, a mixture of cyclopentadiene and 2,3-dimethyl-1,3--butadiene (3 mol. equiv. of each) was used to trap diethyl thioxomalonate (46), generated in situ by heating the anthracene adduct (95) (1 mol. equiv.) in refluxing toluene (Scheme 32). The reaction was complete after 1h and ^{1}H n.m.r. spectroscopy showed the presence of the adducts (93) and (47) in a 3:2 ratio. To consider the value of this result, a control experiment was conducted: the cyclopentadiene adduct (93) was heated in refluxing toluene (Scheme 32) for 1h in the presence of 2,3-dimethyl-1,3--butadiene (3 mol. equiv.). The thione (46) was partially transferred to give a mixture of adducts (93) and (47) in a 2:3 ratio.
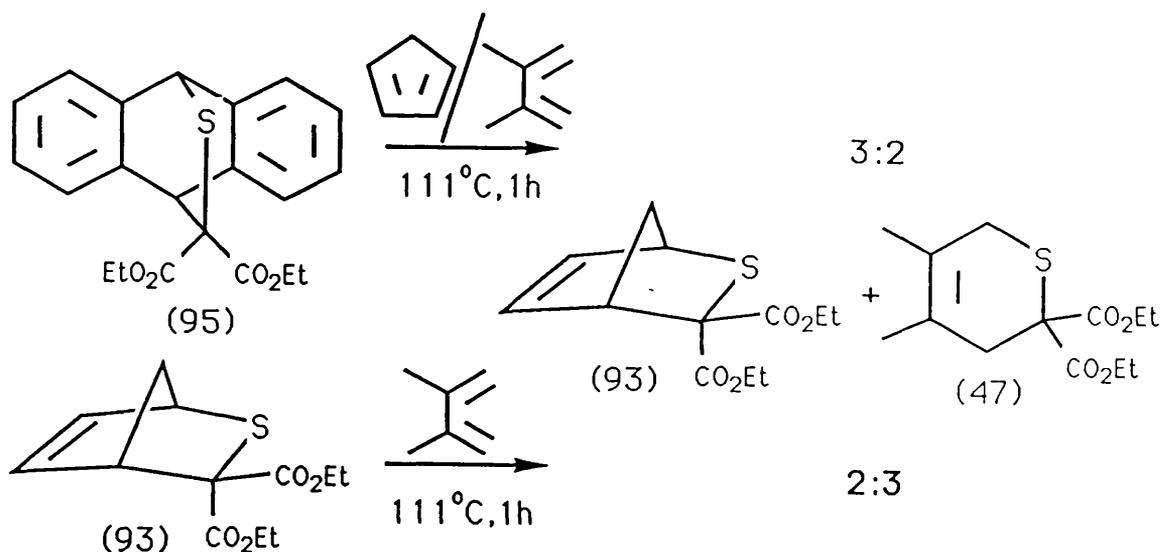
Scheme 32

Clearly then, the essentially quantitative thermal transfer of the thione (46) from the anthracene adduct (95) to the mixture of dienes does not give us the relative rates of cycloaddition of (46) to cyclopentadiene and 2,3-dimethyl-1,3-butadiene. Formation of the bridged, and consequently strained, adduct (93) is reversible while, very probably, the monocyclic adduct (47) is not formed reversibly at the reaction temperature. Thus the obseved 3:2 ratio of (93) and (47) serves only to give a lower limit to the relative rates of reaction of the thione (46) with these dienes.

41

Graph 1.   Determination of rate constant (k) of dissociation of the anthracene adduct (27) of ethyl thioxoacetate (28) at 100°C from the slope of $\ln(A - A_t)$ against time.

A = absorbance at 355nm at 24h.

A_t = absorbance at 355nm at time, t.
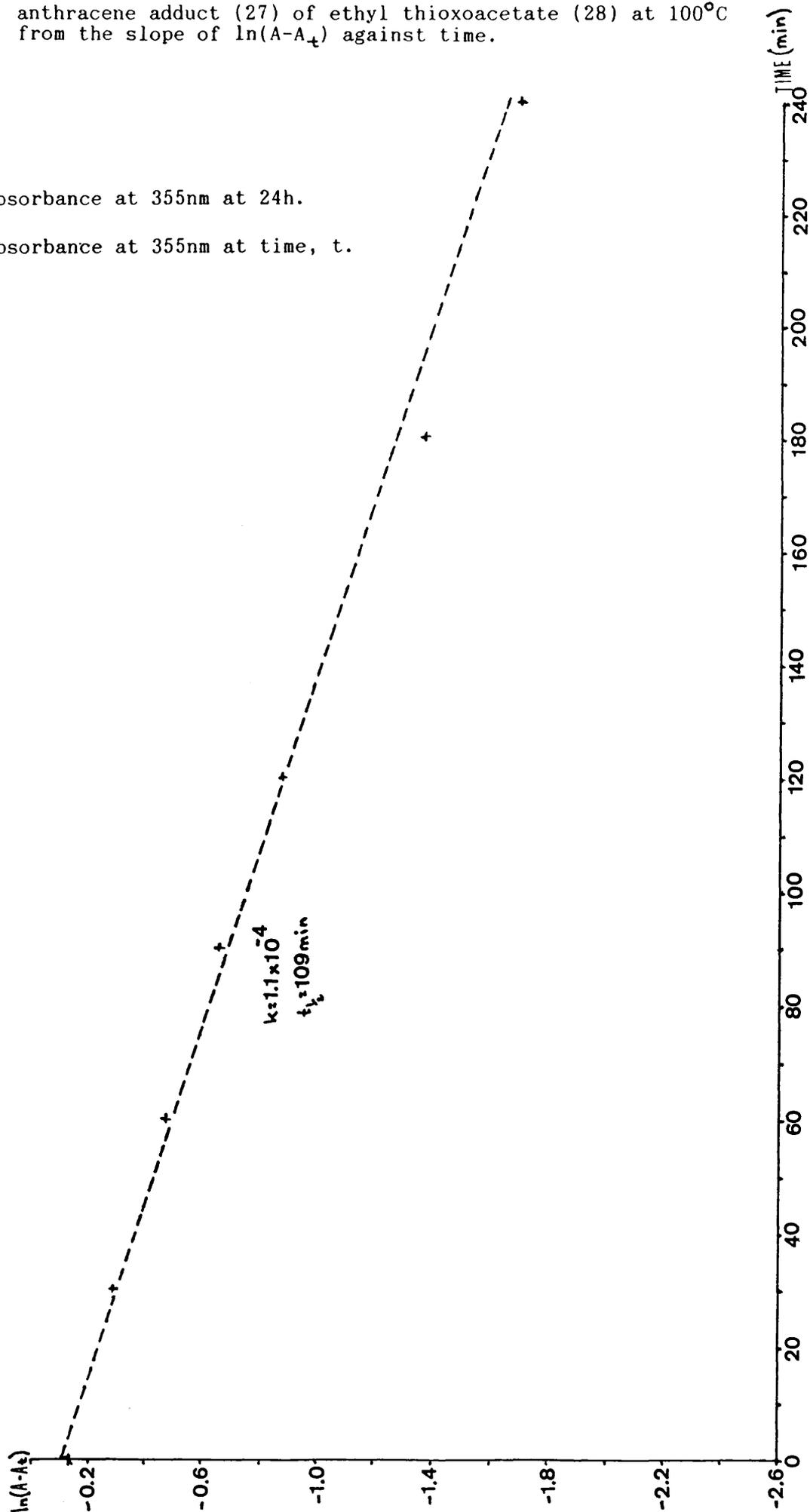
(b)   RATES OF DISSOCIATION OF THE ANTHRACENE CYCLOADDUCTS (27) AND (95).
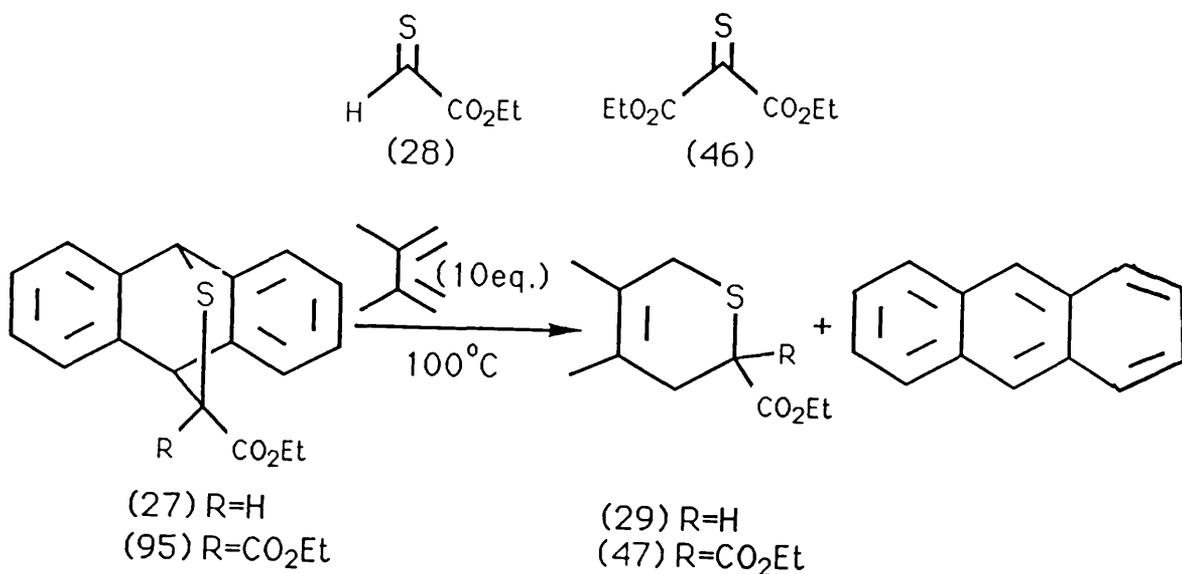
Scheme 33

A series of kinetic experiments[46] were conducted on the transfer of the thioxoacetate (28) and the thioxomalonate (46) (and their S-oxides – see Chapter 2) from their anthracene adducts (27) and (95) to 2,3-dimethyl--1,3-butadiene (Scheme 33). Both reactions were monitored by the ultra--violet absorbance (λ_{max} 355 nm) of the liberated anthracene.

Both transfer reactions were carried out in toluene, at 100°C, with a large excess of 2,3-dimethyl-1,3-butadiene (10 mol. equiv.) in order to

Graph 2.   Determination of rate constant (k) of dissociation of the
            anthracene adduct (95) of diethyl thioxomalonate (46) at 100°C
            from the slope of $\ln(A-A_t)$ against time.

A = absorbance at 355nm at 24h.

A_t = absorbance at 355nm at time, t.
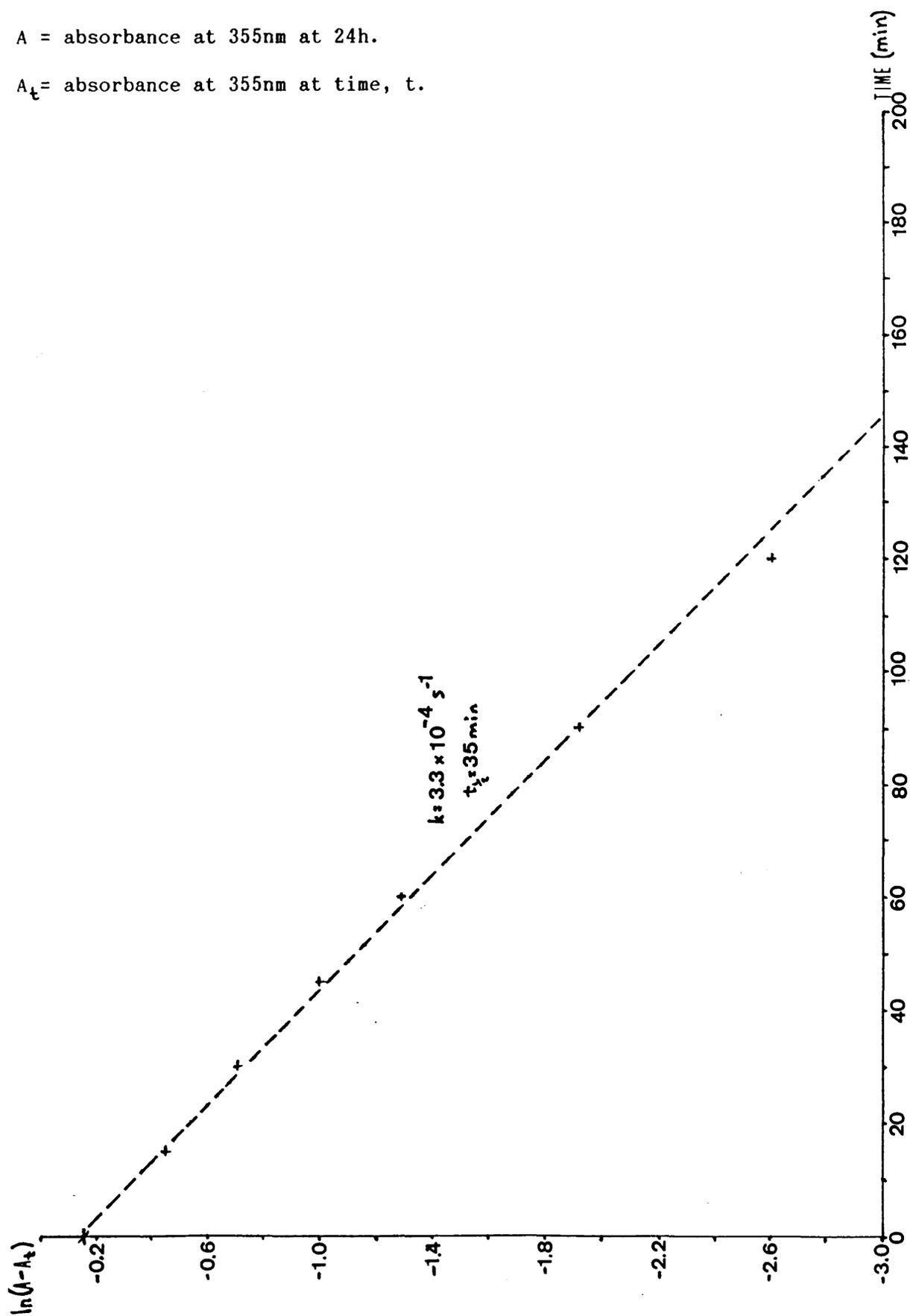
simplify the kinetics. That is, the concentration of this diene did not

diminish significantly during the experiments, and recapture of the

dieneophile (28) or (46) by anthracene is assumed to be insignificant.

Both reactions were shown to follow approximately first-order kinetics,

with respect to the concentration of (95) - see Graphs 1 and 2.

Significantly the measured rate constants (Table 1) show that the presence

of the second ester group in (95) increases the rate of dissociation of

the anthracene adduct (95) by a factor of <u>ca</u>.3 compared with the

anthracene adduct (27).

Table 1. Dissociation rates (k) of the anthracene adducts, (27) and (95),

of ethyl thioxoacetate (28) and diethyl thioxomalonate (46) at

100°C in toluene.

Thiocarbonyl compound	k (s^{-1})	$t_{\frac{1}{2}}$ (min)
Ethyl thioxoacetate (28)	1.1×10^{-4}	109
Diethyl thioxomalonate (46)	3.3×10^{-4}	35

The observation that both reactions obey first-order kinetics

means that the rate determining step is the unimolecular

decomposition of the anthracene adduct.

<u>I.e.</u>

$$\text{anthracene adduct} \xrightleftharpoons[k_{-1}]{k_1} \text{thiocarbonyl compound} \xrightarrow{k_2} \text{2,3-dimethyl-1,3-butadiene adduct}$$

$$k_1 \gg k_{-1} < k_2$$
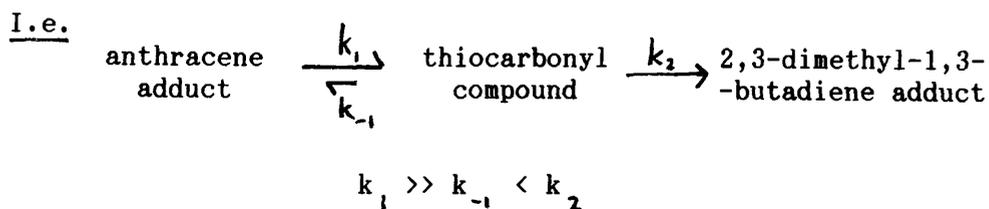
(c) REGIOCHEMISTRY OF DIELS-ALDER ADDITIONS OF DIETHYL THIOXOMALONATE (46)
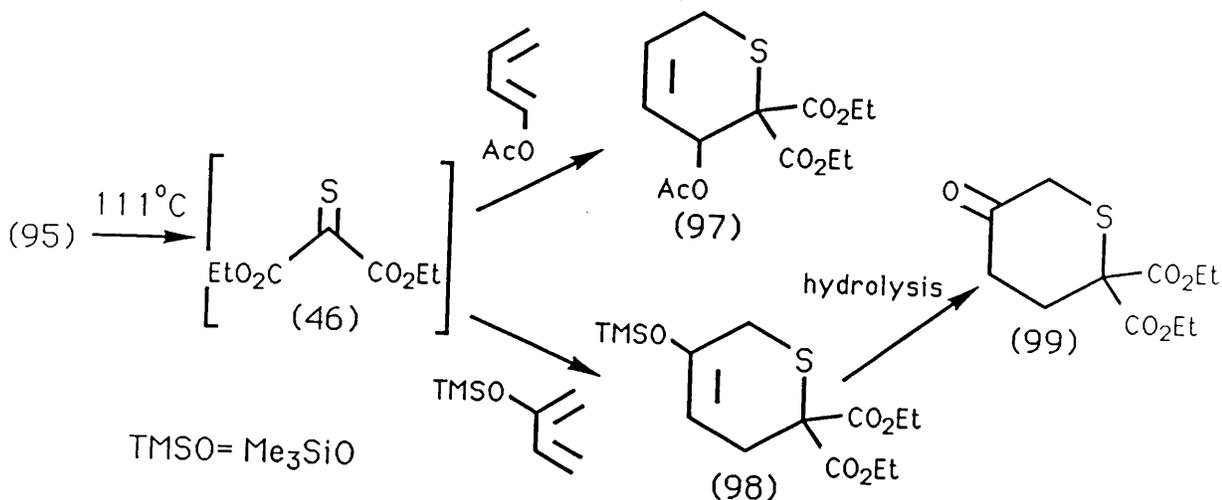
Scheme 34

Diethyl thioxomalonate (46), generated *in situ* by heating the anthracene adduct (95) in refluxing toluene for 1h, reacted with 1-acetoxy-1,3-butadiene (2 mol. equiv.) regiospecifically to give only the adduct (97) and anthracene (Scheme 34). The regiochemistry was determined as discussed in the following section.

Similarly, the thione (46) was trapped *in situ* with 2-trimethylsiloxy--1,3-butadiene (2 mol. equiv.) to give only the moisture-sensitive adduct (98) regiospecifically, which was easily hydrolysed to the ketone (99). Again the regiochemical assignment will be discussed in the following section.

44

		compound			
nucleus	(97) AcO, S, CO₂Et/CO₂Et	(97) a AcO, S, CO₂Et/CO₂Et	(47) S, CO₂Et/CO₂Et	(98) TMSO, S, CO₂Et/CO₂Et	(99) O, S, CO₂Et/CO₂Et
¹H 3-H (H₂)	ca. 6.1	ca. 5.8 ᵃ	2.67 (s)	2.89	2.60 or 2.71
6-H₂	3.61	3.91, 3.23 ᵇ	3.06 (s)	3.12 (s)	3.30 (s)
¹³C 4-H (H₂)			N/A	4.95	2.60 or 2.71
5-H	5.83, 6.15 ᶜ	5.61, 6.08 ᶜ		N/A	N/A

Notes

a   Data supplied by M.S. Rahman [47].

b   Values for each 6-H are averaged between stereoisomers.

c   Assignments are undetermined. All possible values are given.

It is worth noting at this stage that these observed regiospecificities are directly in agreement with the predictions made by frontier molecular orbital (f.m.o.) theory (Scheme 19). The presence of two electron-withdrawing groups, instead of only one as displayed in Scheme 19, on the dieneophile would be expected to enhance the regioselectivity.

Assignment of the regiochemistry of the cycloadduct (97) and the ketone (99).

Assignment of the structures (97) and (99) was made using ^{1}H n.m.r. spectroscopy only. As neither of these adducts are crystalline x-ray structure determination was not possible.

(97)
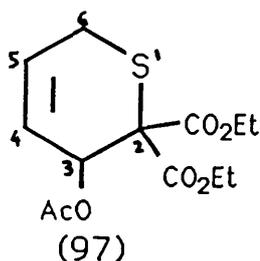
The table of n.m.r. data (Table 2) gives information on five relevant compounds, including the ethyl thioxoacetate adducts[47] (100). The stereoisomers of (100) are very similar to (97), except for the vicinal coupling between the 2-H and 3-H, which allows unambiguous assignment of the regiochemistry of (100). As can be seen from Table 2, the ^{1}H chemical

shifts for the 6-methylene protons and the 3-H in (100) and (97) are very similar. This observation, and also the similar chemical shifts for the 6-methylene protons in (97) and (47), are the basis for assigning the structure (97) to the cycloadduct, having the acetoxy group at the 3- rather than at the 6-position.

TMSO $\cdots$ S' $\cdots$ CO$_2$Et / CO$_2$Et   (98)

O $\cdots$ S' $\cdots$ CO$_2$Et / CO$_2$Et   (99)
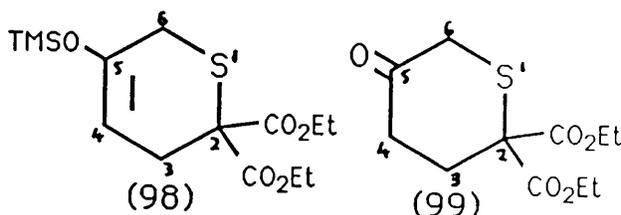
The regiochemistry (98) for this cycloadduct, and the corresponding structure (99) for its hydrolysis product, were also assigned by n.m.r. spectroscopy (Table 2). The signal at δ3.30 in the ^{1}H n.m.r. spectrum of the ketone (99) was a singlet. Its multiplicity and chemical shift indicated that it arose from an isolated 6-methylene group and not from an isolated 3-methylene group, as would arise in the (unknown) 4-oxo regioisomer. This is confirmed by the n.m.r. of the cycloadduct (98) which also shows a singlet with an appropriate chemical shift for the 6-methylene group.

(d)   AN 'ENE' REACTION OF DIETHYL THIOXOMALONATE (46).
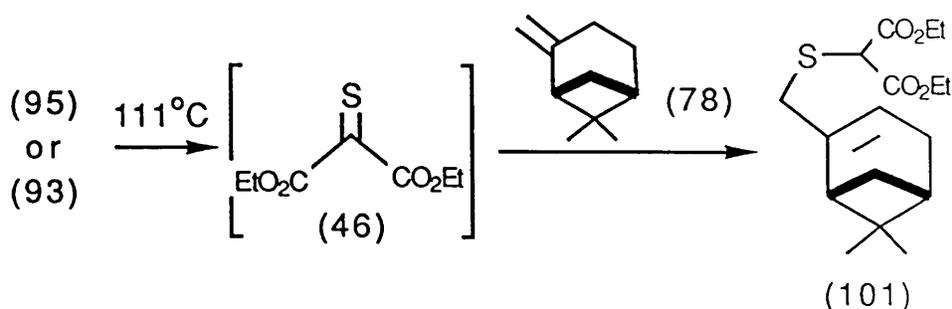
Scheme 35

Both the anthracene adduct (95) and the cyclopentadiene adduct (93)

dissociated in refluxing toluene to liberate the thione (46), which acted

as the 'ene' component in a reaction with (-)-β-pinene (78) (3 mol.

equiv.) to give   (101) as the exclusive product (Scheme 35).

Only C-S bond formation was observed, which is analogous to the findings

of Snider[37] (Scheme 22) with the dithioester (68). This also complements

the finding that ethyl thioxoacetate (28) reacts with (-)-β-pinene (78)

mainly with C-S bond formation[16,36] (Scheme 24).

The anthracene adduct (95) reacted faster, as expected, giving (101) in

61% yield after 1h, but the cyclopentadiene adduct (93) required 4h to

give (101) in a rather lower yield (30%). The structure of the oily

product (101) was established by ^{1}H n.m.r. spectroscopy. In particular,

signals at ∮3.25 [bs,S-C$\underline{H}$] and ∮4.11 [s,S-C$\underline{H}$(CO$_2$Et)] were diagnostic.

The alternative (and unknown) product (102) would have shown corresponding

signals for a methylene group at higher field, and a thiol group,

exchangeable with deuterium oxide, neither of which were observed.

(101)

(102)
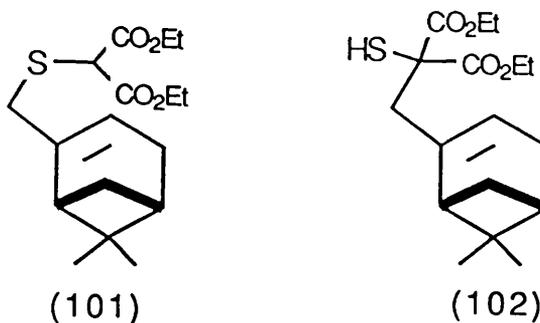
Considering the HOMO of an olefin (103) and the LUMO of the

heterodieneophile (104)[48] , application of simple f.m.o. theory gives a

pictorial representation of the 'ene' reaction shown in Scheme 36.

(103)   (104)   (105)

                                                major
                                                product
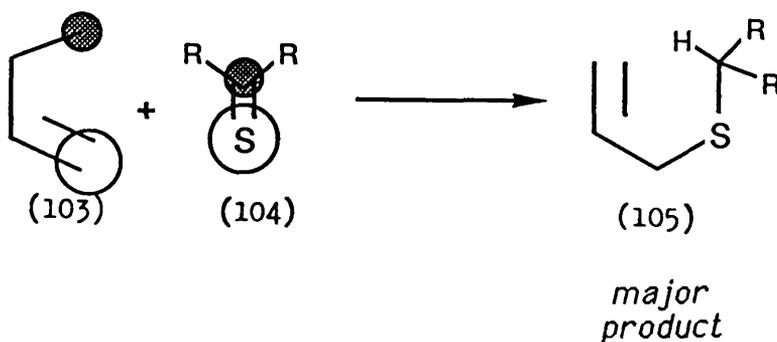
Scheme 36

When one or both of the groups (R) on the thioketone (104) are electron-withdrawing, this lowers the energy of the LUMO, accelerating the reaction. It also reduces the orbital coefficient at carbon, encouraging greater regioselectivity in favour of C-S bond formation.

This accounts for the regiospecificity of the reaction of diethyl thioxomalonate (46) with (-)-β-pinene (78) (Scheme 35), and also for the trends observed in 'ene' reactions of thiocarbonyl compounds. For example, ethyl thioxoacetate (28) reacts with (-)-β-pinene (78) to afford a 4:1 mixture of C-S and C-C formation products (Scheme 24). As expected, thiobenzaldehyde (20) exhibits less selectivity, reacting with (78) to give a 1:2 mixture of products, now fovouring C-C bond formation (Scheme 23), which is analogous to the regiochemical preference shown by ketones in 'ene' reactions.[38]

CONCLUSIONS.

The cyclopentadiene adduct (93) and particularly the anthracene adduct (95) of diethyl thioxomalonate (46) are useful auxiliary precursors, liberating the electrophilic thioketone (46) on heating. This thione (46) can be 'transferred' to other dienes quantitatively, or can react with (-)-β-pinene (78) in an 'ene' reaction. Both the Diels-Alder cycloadditions of diethyl thioxomalonate (46) to unsymmetrical dienes and also the 'ene' reaction, were regiospecific; only a single product was detected in each case.

CHAPTER 2

"THE SYNTHESIS AND REACTIONS OF DIETHYL THIOXOMALONATE S-OXIDE."

INTRODUCTION

STABILITY OF SULPHINES.

Sulphines (106), or thiocarbonyl S-oxides, are more stable than their thiocarbonyl equivalents (107). This is related to the strength of the C-S π-bond. The overlap between the carbon 2p and the sulphur 3p orbitals is better in sulphines than in thiocarbonyl compounds because the positive charge on the sulphur atom in sulphines reduces the energy of the 3p orbital. This makes it more similar in size and energy to the carbon 2p orbital, improving orbital overlap.

(106)   (107)
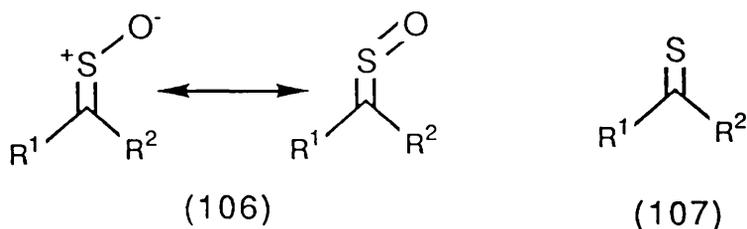
Because the C-S-O system is bent[49] sulphines can exist in two geometric forms[50]. These Z and E forms are not readily interconvertible, indicating a significant double bond character between the carbon and sulphur.

Consideration of the more recent reviews on sulphine chemistry indicates that the same trends apply to sulphines as to thiocarbonyls in

how the stability of the moiety is affected by substituent groups.

Electron-donating groups tend to stabilise sulphines: thus the $\underline{S}$-oxides of thioamides[56,57] (108) and dithioesters[11,58,59] (109) are especially stable.

(108) X=NR^3

(109) X=S

R^1,R^2,R^3,= H, alkyl, aryl
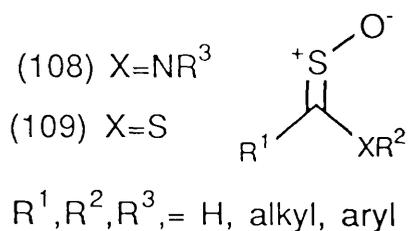
Conversely, electron-withdrawing groups destabilise sulphines, as they do thiocarbonyl compounds, and examples of highly reactive and unstable sulphines with attached ketonic[55,60] (110), or ester groups[55,61] (111) are to be found in the chemical literature.

(110) Z=COR^2

(111) Z=CO$_2$R^2

R^1= H, alkyl, aryl

R^2= alkyl, aryl
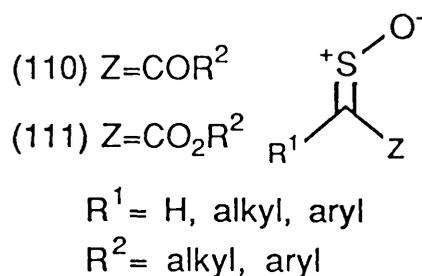
Several examples of sulphines stabilised by steric crowding have been synthesised, such as fluorenylidene sulphine[62] (113), which was made by 1,2-dehydrochlorination of the sulphinyl chloride (112) with base (Scheme 37). Another example is di-t-butyl sulphine (115) which can be made from the thione (114) by treatment with either a peracid[63] or ozone[64] (Scheme 37). Both are crystalline and are stable for several days.
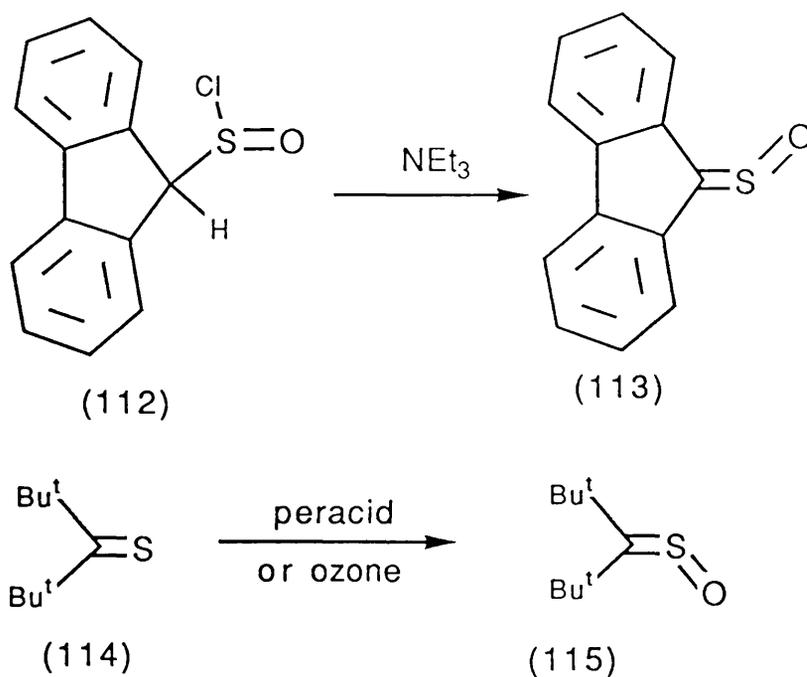
Scheme 37

THE DISCOVERY AND SYNTHESIS OF SULPHINES.

Sulphines have been of interest to chemists since 1923 when Wederkind

et al sythesised the stable sulphine[65] (119) by a rather esoteric

reaction of camphor-10-sulphonyl chloride (116) with base (Scheme 38); the

structure remained uncertain until settled in 1963 by King and Durst[66].
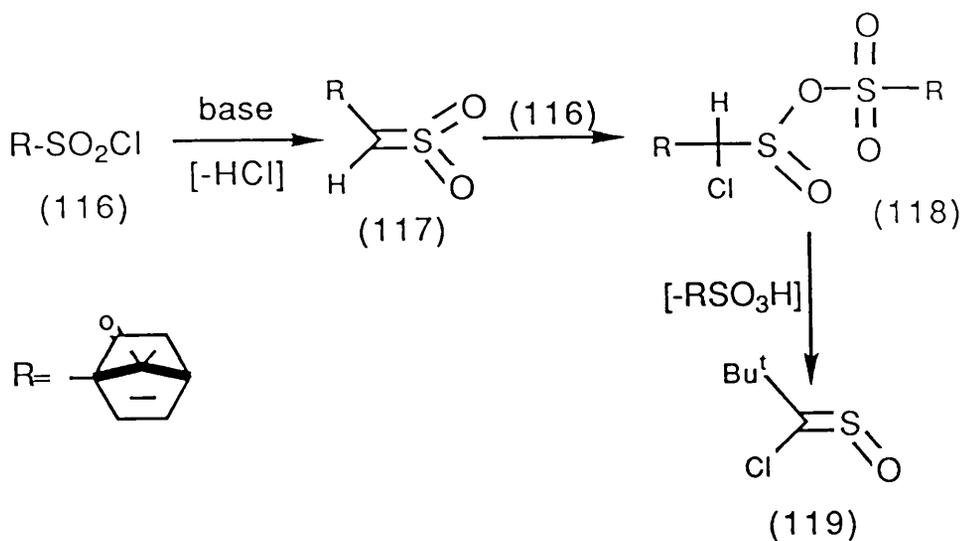
Scheme 38

A more direct sythesis of stable sulphines (Scheme 39) was achieved by
Kitamura[67] in 1938 who used hydrogen peroxide to oxidise thioamides (1),
although the correct structure of their products was not deduced until
1960 by Walter[68].

(1)   (120)

R= Ph, CH₂Ph
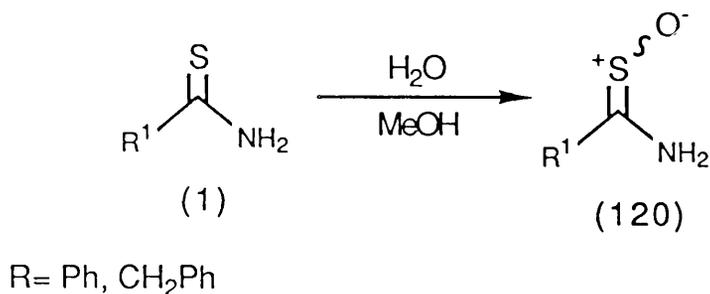
Scheme 39

Sulphine chemistry became of biochemical importance in the 1960's with
the discovery by Wilkens that thiopropanal S-oxide (121) is the
lachramatory factor in onions[69], and the subsequent discovery that
thioacetamide S-oxide (122) is a metabolite of thioacetamide (123), and is
toxic. As a result thioacetamide was banned from use as a preservative
for citrus fruit[57].

(121)   (122) X= SO
                   (123) X=S
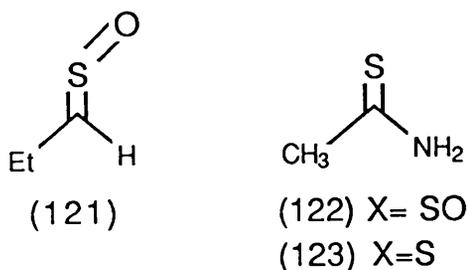
The first synthesis of a thioketone S-oxide was achieved in 1964 when Sheppard and Dieckmann[62] synthesised (113), as already discussed (Scheme 37). An analogous reaction gave the first thioaldehyde S-oxide (124) to be synthesised[62] (Scheme 40).
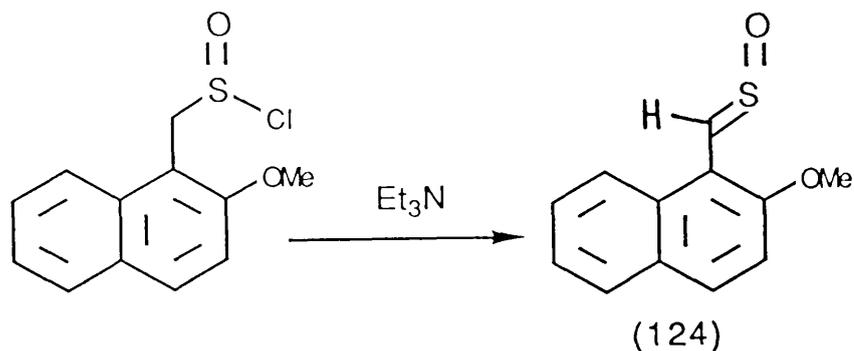
Scheme 40

GENERATION OF SULPHINES BY RETRO-DIELS-ALDER REACTION.

The first generation of a sulphine by the retro-Diels-Alder reaction was achieved by Elsasser and Sundermeyer[70] in 1985. They generated the sulphine (126) quantitively by heating its anthracene adduct (125) at 180°C (Scheme 41).

(126)

(125)
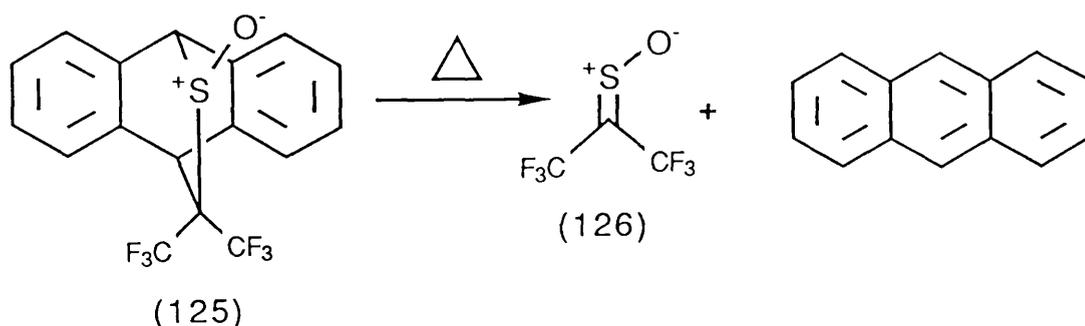
Scheme 41

In 1987 it was shown[61] (Scheme 42) that the _trans_-anthracene adduct (127) dissociated reversibly at 60°C to liberate the (_E_)-sulphine (129) and that the _cis_-anthracene **adduct** (128) dissociated reversibily at 80°C to liberate the (_Z_)-sulphine (130). In both cases the released sulphines were trapped _in situ_ with 2,3-dimethyl-1,3-butadiene, in high yields, to give the adducts (131) and (132) with retention of stereochemistry. Only the (_E_)-sulphine was successfully trapped _in situ_ with cyclopentadiene to give (133) and with thebaine (40) to give (134), both in high yields.

The trans-cyclopentadiene adduct (133) was isomerised with base to the

cis-adduct (135). Both of these adducts, on heating, liberated a sulphine,

which was trapped in situ by 2,3-dimethyl-1,3-butadiene. The

trans-cyclopentadiene adduct (133) gave only the trans-product (131) but

the cis-cyclopentadiene adduct gave a mixture of cis- and trans-products

(131) and (132).
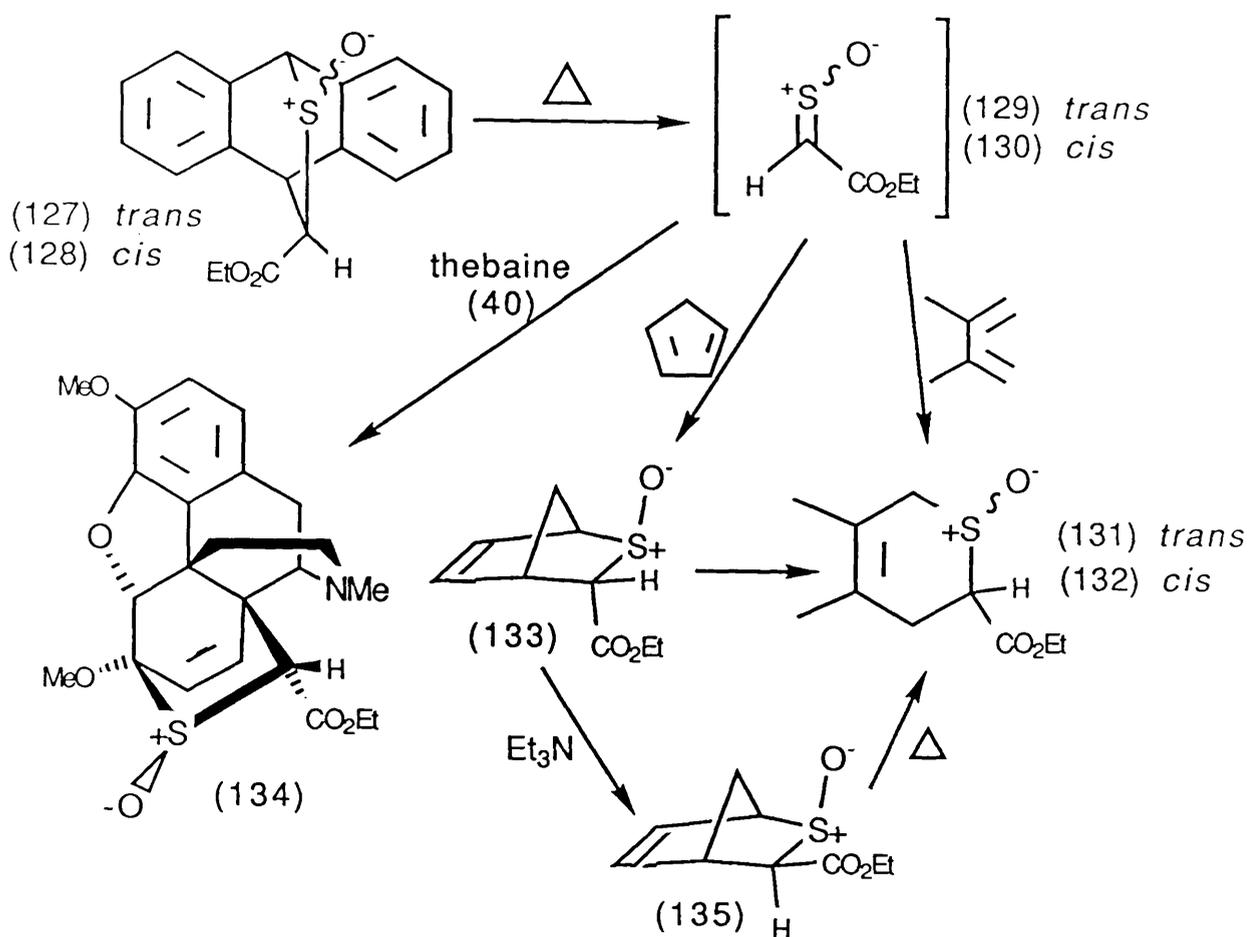
Scheme 42

SYNTHESIS OF ANTHRACENE AND CYCLOPENTADIENE ADDUCTS OF SULPHINES.

The anthracene adduct (125) of bis(trifluoromethyl) sulphine (126) was

most easily synthesised[71] (Scheme 43) by the oxidation of the

Diels-Alder cycloadduct (136) of hexafluoroacetone with

m-chloroperoxybenzoic acid (mCPBA).

(136)   (125)
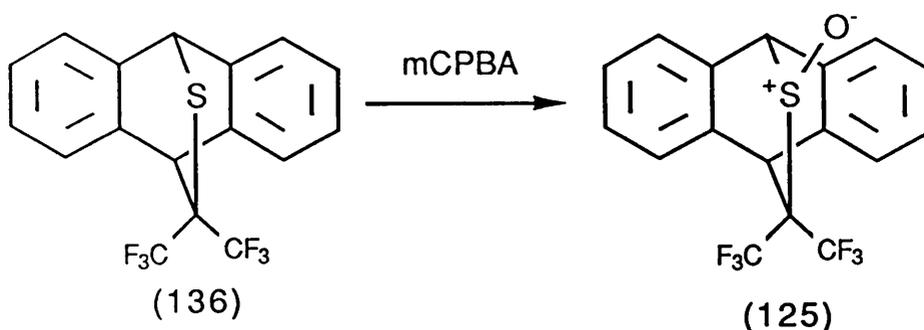
Scheme 43

Similarly the cycloadducts of ethyl thioxoacetate S-oxides (129) and

(130) were synthesised[61] by oxidation of the corresponding sulphides

with mCPBA. The ratios of trans- to cis-oxides are given in Scheme 44.

As can be seen trans-S-oxides are generally predominant. However in the

cyclopentadiene case, the only reported cyclopentadiene adducts both have

the S-O bond exo even though this gives a cis-S-oxide in the case of (135).

RATIO (*trans* : *cis*)

2.5 : 1

(127) *trans*
(128) *cis*

trans only

cis only

(131) *trans*
(132) *cis*

4 :1

trans only
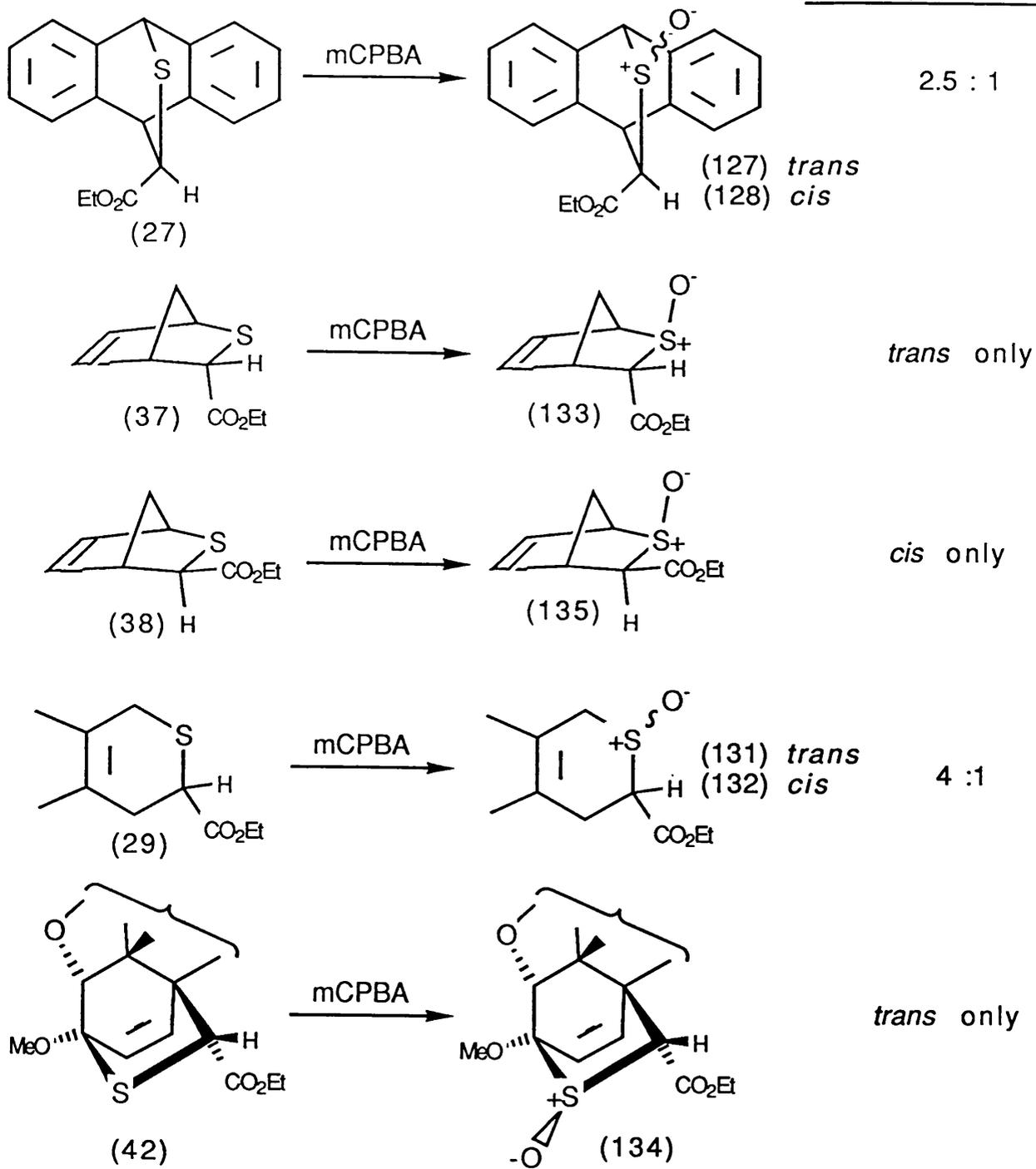
Scheme 44

Similarly, Block and Wall[72] showed that the sulphide (137) gave only

the exo-S-oxide (138) when treated with mCPBA (Scheme 45), and that the

adduct was stable to prolonged heating and so was useless as a source of

(E)-propane sulphine (139). They also showed that (Z)-propane sulphine

(140) could be trapped in situ with cyclopentadiene at -78°C to give the

cis-cyclopentadiene adduct (141)with the S-O bond endo. However at 0°C

the adduct (141) underwent a [2,3]-sigmatropic rearrangement to give the

stable sultene (142) quantitatively.
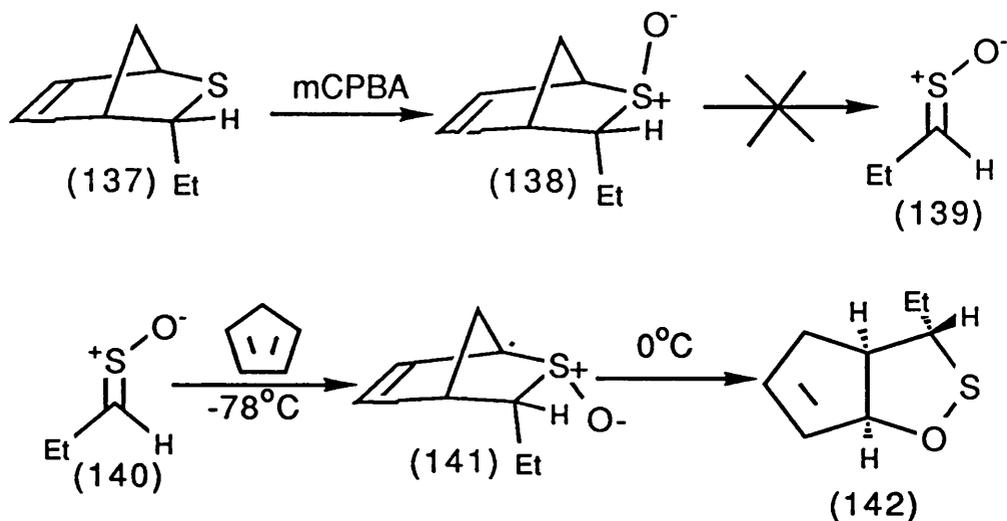
<p style="text-align:center"><u>Scheme 45</u></p>

α-OXOSULPHINES.

α-oxosulphines[51] , other than those derived from thioamides[56] , are

highly reactive species and are usually "trapped" in pericyclic reactions

to give stable derivatives. An example illustrating a general route

to such species is shown in Scheme 46. The silyl enol ether (143) was

treated with thionyl chloride to give the unstable sulphine (144) which was

then trapped in situ to give the heterocyclic product (145) by Diels-Alder

cycloaddition. The entire reaction sequence was carried out at 20°C or

below.

Alternately, α-oxosulphines can be generated from retro-Diels-Alder

reactions of appropriately labile cycloadducts[61] (Scheme 42).

Scheme 46   (145)
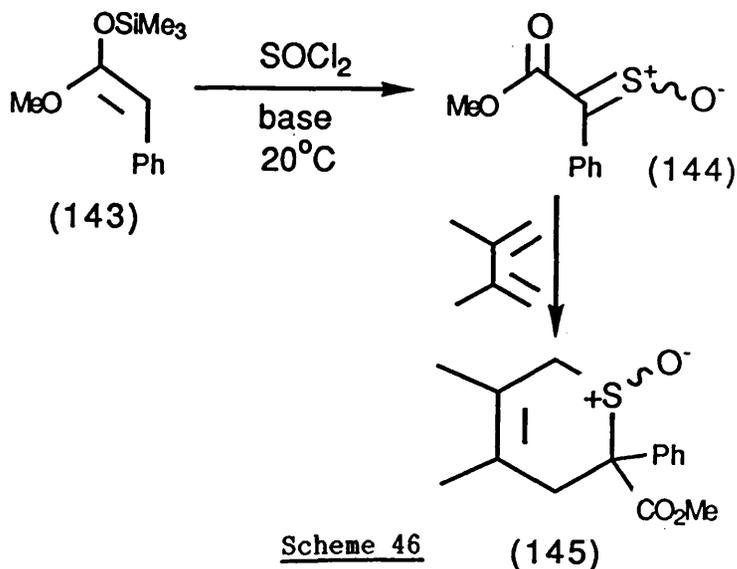
THIOXOMALONATE S-OXIDES.

The electron-withdrawing groups attached to the sulphine residue of

thioxomalonates, e.g. (148), considerably destabilises the molecule. For

this reason references to thioxomalonate S-oxides are relatively rare in

the chemical literature. The first synthesis of a thioxomalonate S-oxide

was by Rozendaal and Zwanenburg [55,73] in 1985 (Scheme 47) who treated the

silyl enol ether (146) with thionyl chloride to give the desired sulphine

(148) which reacted in situ with 2,3-dimethyl-1,3-butadiene to give the

S-oxide (149) in 53% yield. Care must be taken to avoid the unwanted

side-reaction of the silyl enol ether (146) with the intermediate

sulphinyl chloride (147) to give (150).
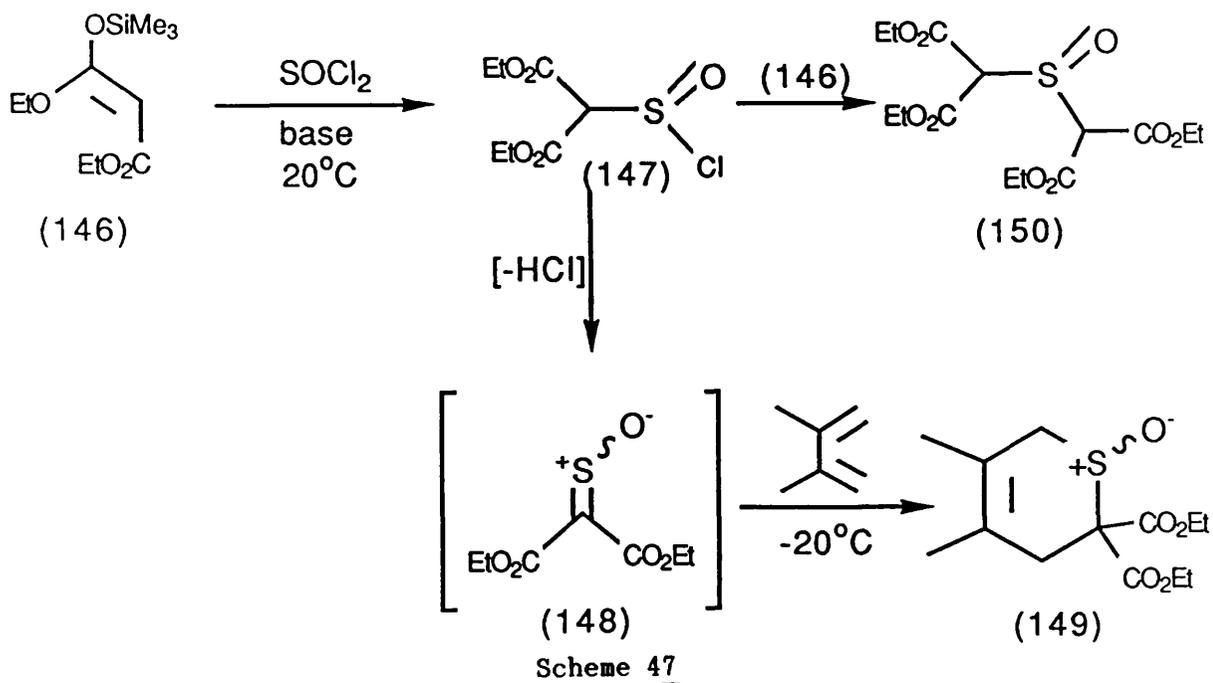
Scheme 47

At almost the same time, Saalfrank and Rost [74] published an alternative
synthesis of the sulphine (148) from the reaction of the allene
(151), a malonic ester dianion equivalent, with thionyl chloride (Scheme
48). The initially formed sulphinyl chloride (152) gave the thioxomalonate
S-oxide (148) which was trapped at -50°C with 2,3-dimethyl-1,3-butadiene
to give the sulphoxide (149) in 42% yield.
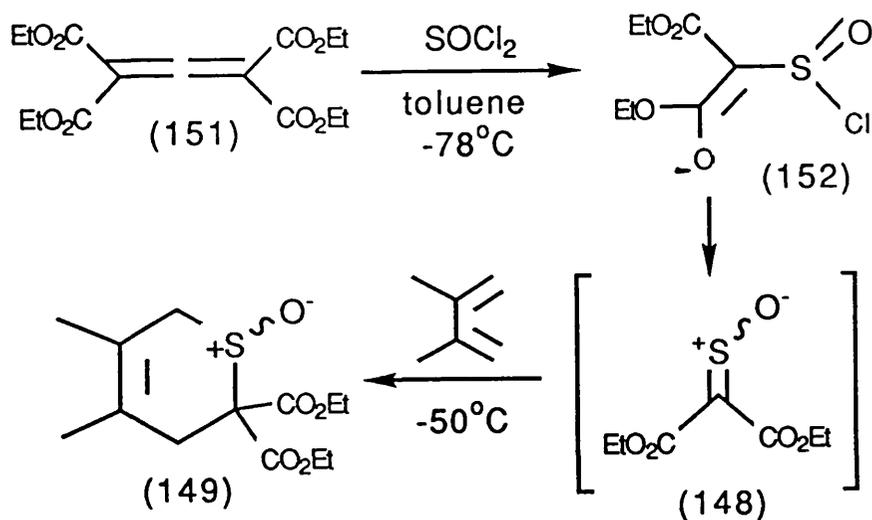
Scheme 48

The most notable byproduct of this reaction was tetraethyl ethene

tetracarboxylate (155), which is presumed to be formed (Scheme 49) via the

sulphine dimer[75]   (153) by elimination of sulphur dioxide to give the

episulphide (154), then by loss of sulphur[76] to give the olefin (155) in

31% yield.
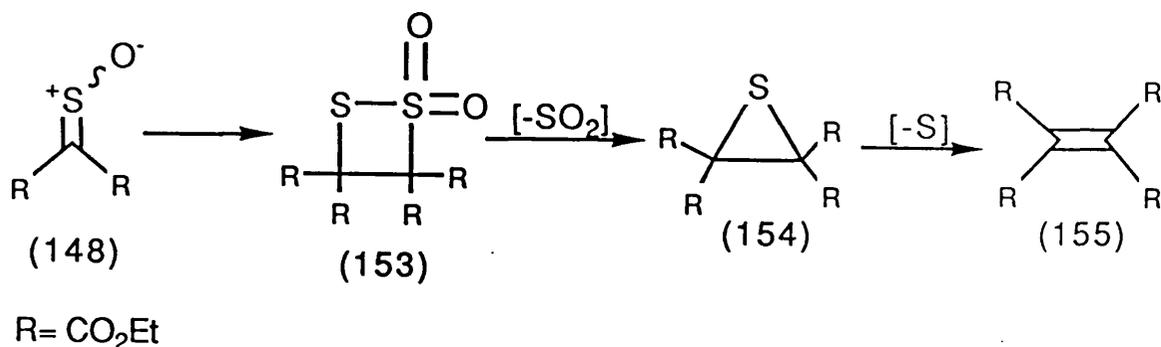
Scheme 49

Supporting evidence for this side-reaction is the thermal decomposition

(Scheme 50) of the sulphine (126) to give the alkene[54]   (156).
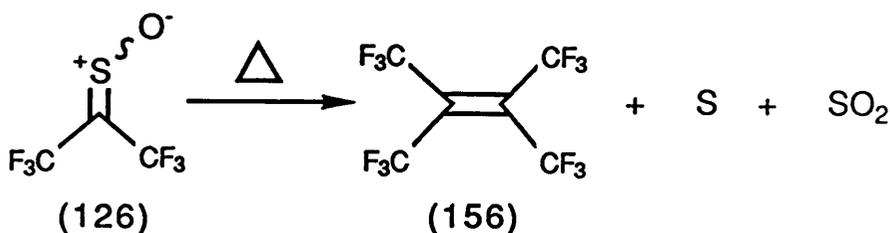
Scheme 50

The heterocycle (47) was also produced as a byproduct, in 22% yield, by reduction of the S-oxide (149). It was suggested by the authors that this reduction was effected by elemental sulphur (produced in Scheme 49) but it seems more likely that the excess of thionyl chloride used is the reducing agent[77] in this case.

REACTIONS OF SULPHINES.

Most of the studies on sulphine chemistry have been conducted on stable sulphines [51-55] and, in general, the reactions of sulphines are quite markedly different from those of the corresponding thiocarbonyl compounds. A characteristic reaction of many sulphines (106) is the loss of elemental sulphur (Scheme 51) to give ketones [53] (158), presumably via the oxathirane (157). This contrasts with the decomposition shown in Schemes 49 and 50 to give olefins which is the preferred mode of decomposition of sulphines with electron-withdrawing groups.
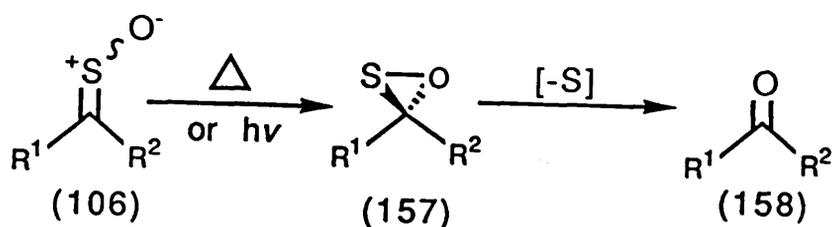
Scheme 51

Other common reactions of sulphines (106) include their reduction to thiocarbonyl compounds (107) with either P_2S_5 or $PSBr_3$ [78] (Scheme 52).
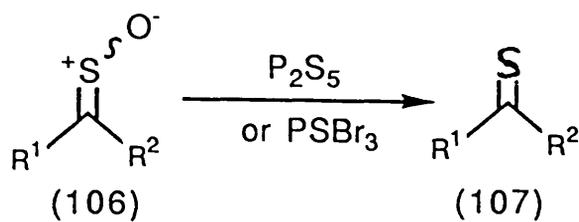
Scheme 52

(a)   REACTIONS OF SULPHINES WITH NUCLEOPHILES.

Attack at sulphur (Scheme 53) is usual in reactions of sulphines (106)

with nucleophiles. For example, aryl- and alkyl- lithium reagents react

with sulphines to give carbanions (159), which can be quenched with water

to give sulphoxides (160) in high yields[78,79]. Reactions of sulphines with

an electrophile (E[+]) give products substituted at carbon[80] (161).
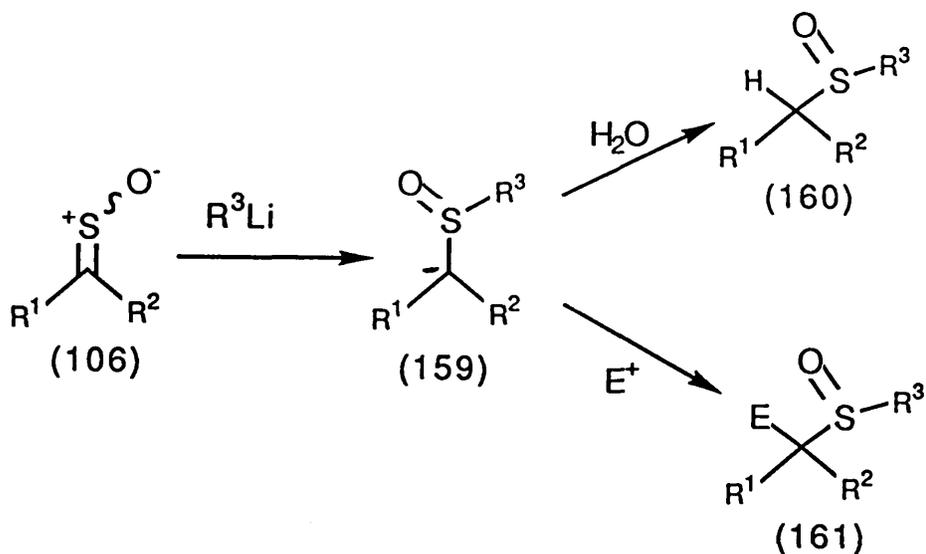
Scheme 53

Much less common are reactions involving nucleophilic attack at the

sulphine carbon. One such reaction is the hydrolysis of sulphines (106)

(Scheme 54). Protonation of the sulphine sulphur atom (under acidic

conditions) is followed by nucleophilic attack at carbon by water to give

a ketone [53] (158). Alternatively, for sulphines with an

electron-withdrawing group (162) a reduction product is obtained, under

neutral conditions, by nucleophilic attack by water at carbon and

subsequent expulsion of sulphur dioxide to give a product containing a

methylene group [55] (163).

(106)   (158)

(162)   (163)
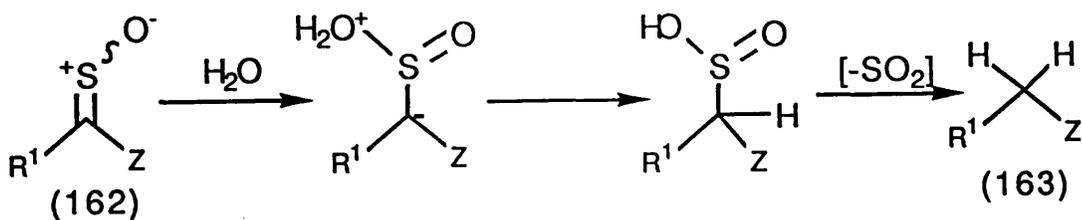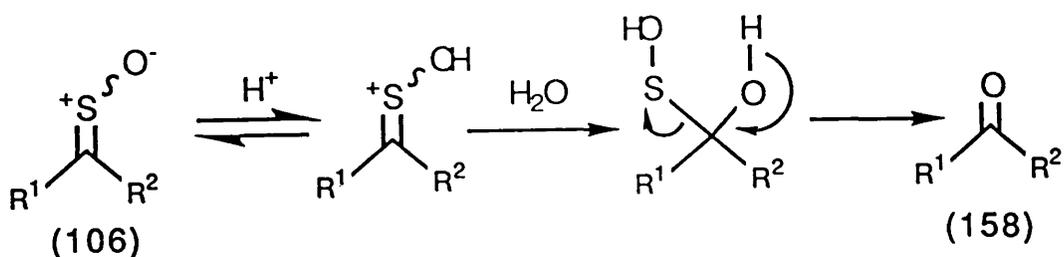
Z = electron-withdrawing group

Scheme 54

(b)   REACTIONS WITH CONJUGATED DIENES.

Because sulphines can exist as $\underline{Z}$ and $\underline{E}$ geometric isomers [50] the

stereochemistry of their cycloadditions is of paticular interest. With

2,3-dimethyl-1,3-butadiene as the 4π- component (Scheme 55), it is

observed that the stereochemistry of the sulphine (106) is predominately

retained [81] in the Diels-Alder cycloadduct (164). Electron-withdrawing

groups enhance the reactivity, and sterically bulky groups retard the

reactivity, of sulphines in Diels-Alder reactions [53] .
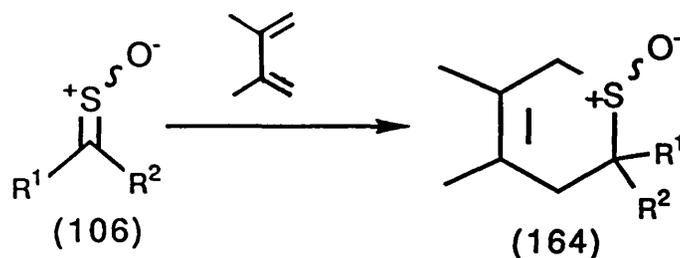
Scheme 55

Regioselectivity of Diels-Alder Reactions Involving Sulphines.

Calculations on sulphines[82] indicate that they are best represented as zwitterions (148) with a positive charge on sulphur and a negative charge on oxygen. If it is then assumed that the orbital coefficients on the sulphur are reduced by the presence of a positive charge, it becomes very difficult to make predictions about the relative magnitudes of the C,S and O coefficients in the π-system. In particular, calculations[83] indicate that the LUMO coefficients of sulphines are very similar in magnitude over the three atoms. Thus it is difficult to apply elementary frontier molecular orbital theory to the cycloaddition reactions of sulphines in order to predict the regiochemistry of Diels-Alder reactions involving asymmetric dienes.

(148)
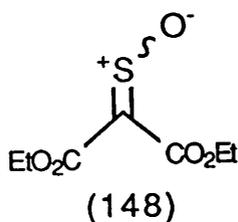
One example of such a cycloaddition is the reaction of dichlorosulphine (165) with 2-(trimethylsiloxy)-1,3-butadiene (Scheme 56) to give the adducts (166) and (168), which are readily hydrolysed to (167) and (169).[53] The major product was shown to be (169).

TMSO= Me₃SiO
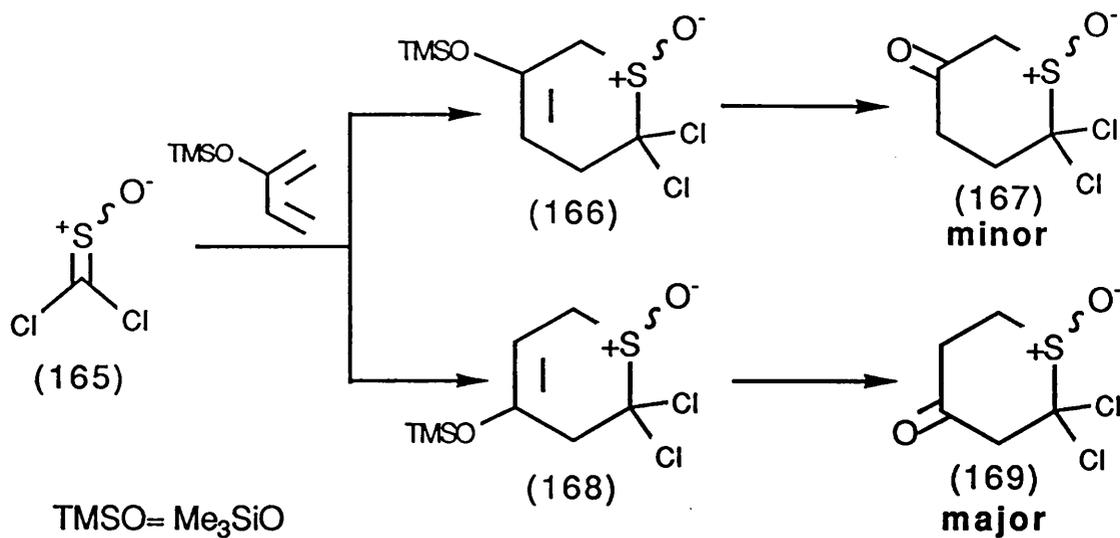
Scheme 56

(c)   REACTIONS WITH MONO-OLEFINS.

Sulphines with an ∝-oxo group can act as the 4π- component in [4+2]-

-cycloaddition reactions with electron-rich olefins[77] . For example,

(Scheme 57) ethyl vinyl ether reacted with the sulphine (170), which is

stabilised by delocalisation , to give the sulphoxide (171) in good yield.
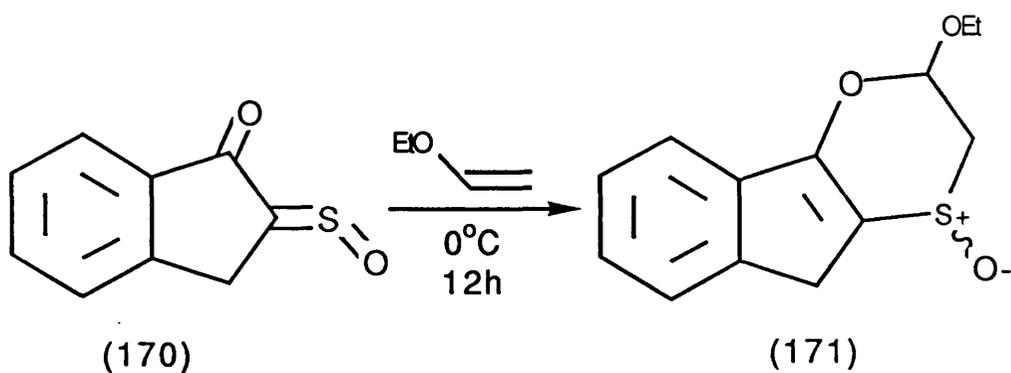
Scheme 57

DISCUSSION

SYNTHESIS OF THE CYCLOADDUCTS OF DIETHYL THIOXOMALONATE S-OXIDE (148).

The chemistry of diethyl thioxomalonate S-oxide (148) has not been extensively studied, despite the synthetic flexibility associated with malonate systems.

$$EtO_2C \quad CO_2Et$$
(148)
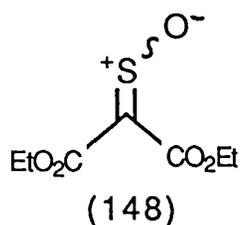
It is, of course, highly reactive because the two electron-
-withdrawing groups considerably destabilise the sulphine system.
The synthesis of (148) has, however, been made both by
1,2-dehydrochlorination of a sulphinyl chloride[74] , and also from
a silyl enol ether[73] , both of which are well documented general
routes [51-55]   for making sulphines. Moreover, it was desirable
to produce a convenient labile precursor which would allow the
sulphine (148) to be generated, reversibly, in situ under neutral
conditions.

The projected labile adducts of the sulphine (148) were
quantitatively synthesised, in the first instance, not by
cycloadditions involving (148), but by oxidation, at room
temperature, of the corresponding adducts (95) and (93) of diethyl
thioxomalonate (46) (Scheme 58). The adduct (149), a non-labile

product of trapping (148) with 2,3-dimethyl-1,3-butadiene, was
synthesised likewise.[73,74]
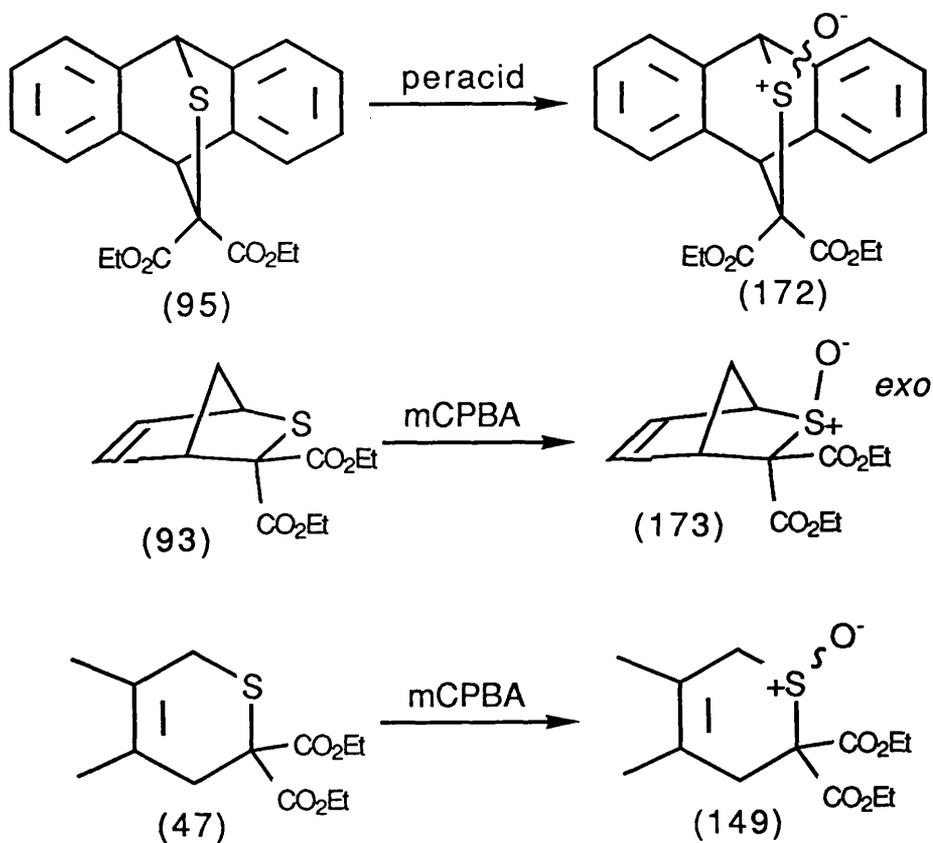
Scheme 58

In each case only a single product was obtained. In the

cyclopentadiene case, oxidation of (93) could potentially give two

products, either or both of the exo- and endo-S-oxides. However,

only the exo-S-oxide was produced, which is analogous to various

Table 3.   ¹H n.m.r. data for the exo-cyclopentadiene adduct (173) and related adducts (133) and (135). [δ (CDCl₃)]

Compound / Nucleus	(173)	(133) endo	(135) exo
7-Hₐ	2.35(dt, J 12,2Hz)	2.26(dt, J 11,3Hz)	2.28(dq, J 11,ca.2Hz)
7-Hᵦ	3.04(d, J 12Hz)	2.51(d, J 11Hz)	2.86(d, J 11Hz)
Δ(δHₐ-δHᵦ)	0.69	0.25	0.58

literature reports [61,72] where exo-S-oxidation of cyclopentadiene

adducts was found to be preferred. It is difficult to say why this

is the case, but exo-adducts of cyclopentadiene are generally

thermodynamically preferred, and so steric control of the oxidation

would seem to be operating.
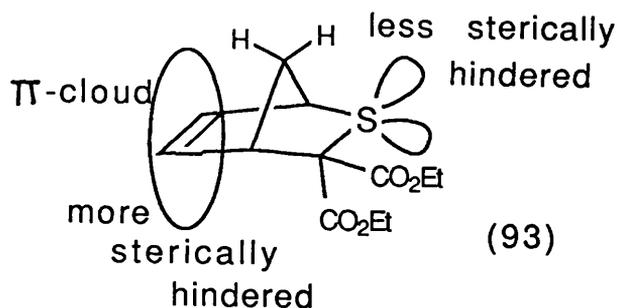
The stereochemistry of (173) was assigned as an exo-S-oxide by

comparison of the ^{1}H n.m.r. with reference compounds (Table 3).

The 7-H_2 was most informative. Note particularly the large

separations (0.58 and 0.69) between the 7-H_a and -H_b signals in

(135) and (173). If the S-O bond in (173) were endo this

separation would be much smaller (cf. (133) where the

endo-ethoxycarbonyl group gives a small $\Delta(\delta H_a - \delta H_b)$ for the 7-H_2).

The cyclopentadiene adduct (93) and the

2,3-dimethyl-1,3-butadiene adduct (47) were both repeatably

oxidised with m-chloroperoxybenzoic acid (mCPBA) in dichloromethane

to give the S-oxides (173) and (149) quantitatively. However,

oxidation of the anthracene adduct (95) proved to be more erratic.

Although the anthracene addut (95) was successfully oxidised
to the S-oxide (172) with mCPBA in dichloromethane at room
temperature, this reaction eventually proved to be irreproducible.
This coincided with renewing the supply of mCPBA. Neither washing
the mCPBA with a phosphate buffer[84] , nor titrating it to take
account of its percentage purity (ca. 70-80% w/w), facilitated the
repeated oxidation of (95). Curiously, this new batch of mCPBA did
succesfully oxidise the cyclopentadiene adduct (93).

This problem was eventually circumvented by changing the peracid
used. Instead of mCPBA, a solution of peracetic acid (ca. 30% w/w)
was used to oxidise the anthracene adduct (95). Although this
reaction was, for a time, successful using dichloromethane as a
solvent, again on renewing the supply of the peracid, attempts to
reproduce previous oxidations failed. Distillation of the peracid
and titration of the distillate failed to eliminate this problem.
Inexplicably, when the solvent was changed   from distilled
dichloromethane to distilled diethyl ether, the S-oxidation of (95)
with peracetic acid (distilled) proceeded successfully and has
since proven consistently reproducible.

GENERATION OF (148) BY RETRO-DIELS-ALDER REACTION.

(a) TRAPPING THE SULPHINE (148) WITH 2,3-DIMETHYL-1,3-BUTADIENE.

Both the anthracene adduct (172) and the cyclopentadiene adduct
(173) dissociated when heated to liberate the sulphine (148),
reversibly, which was trapped in situ with 2,3-dimethyl-1,3-
-butadiene (Scheme 59) to give the cycloadduct (149). As would be
expected from the behaviour of the S-oxides of ethyl thioxoacetate
adducts (Scheme 42), the anthracene adduct (172) dissociated faster
than the cyclopentadiene adduct (173), the former dissociating in
refluxing benzene (80°C) and the latter in refluxing toluene
(111°C). A small amount (ca.5%) of the sultene (174) was also
produced in the reaction from (173). The mechanism by which this
was produced will be discussed in the following section (Scheme
61).
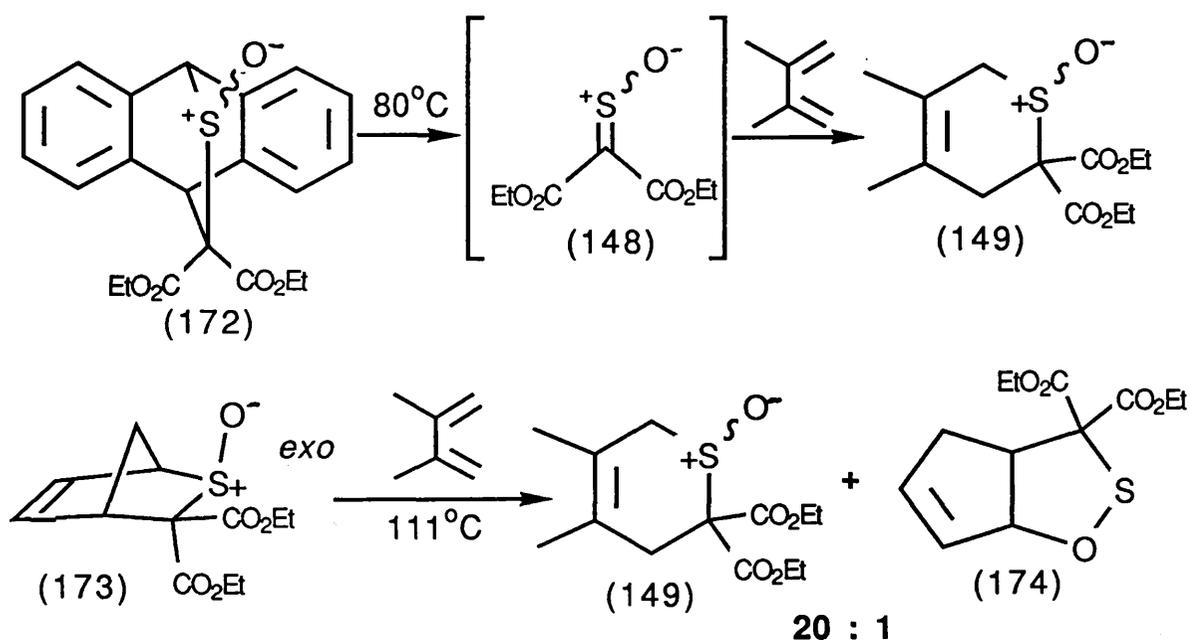
Scheme 59

(b)   TRAPPING THE SULPHINE (148) WITH CYCLOPENTADIENE.

The anthracene adduct (172) liberated the sulphine (148), in

refluxing benzene, which was quantitatively transferred over 1h to

cyclopentadiene (5 mol. equiv.) to give a 2:1 mixture of products

(Scheme 60). The product ratio was determined by ^{1}H n.m.r.

spectroscopy at 200MHz and the products determined to be the

exo-cyclopentadiene adduct (173) (major product) and the sultene

(174) (minor product). The sultene is presumably produced by a

[2,3]-sigmatropic rearrangement of the endo-cyclopentadiene adduct

(175) (not detected) as shown in Scheme 61. When (173) was heated

in refluxing benzene with excess 2,3-dimethyl-1,3-butadiene for 1h,

no (149) was formed indicating that the exo-cyclopentadiene adduct

(173) is stable in refluxing benzene. It is not known whether the

endo-cyclopentadiene adduct (175) dissociates at this temperature

or simply rearranges. In refluxing toluene, heating (172) with

2,3-dimethyl-1,3-butadiene (5 mol. equiv.) gave only the sultene

(174) (Scheme 60).
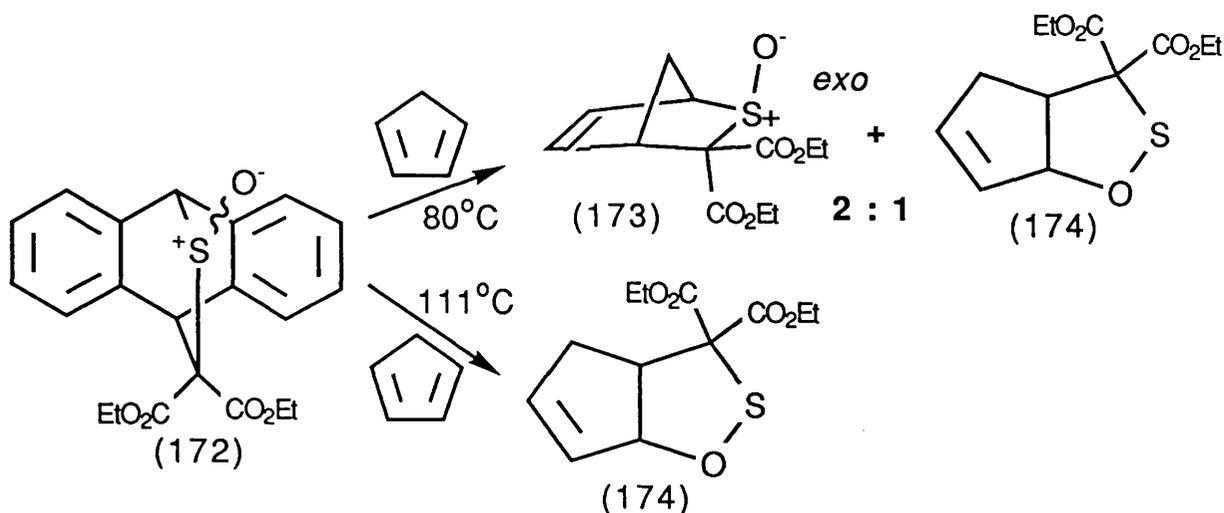
Scheme 60

The cyclopentadiene adduct (173) on heating in refluxing toluene,

over 1h, gave the sultene (174) quantitatively. Presumably, this

involves generation of the sulphine (148), which could be trapped

by liberated cyclopentadiene to give either the exo- or

endo-adducts. The endo-adduct (175) then could undergo a

[2,3]-sigmatropic rearrangement[72] (Scheme 61) to give the stable

sultene (174). This thermodynamic "potential well" means that an

equilibrium mixture of exo- and endo- adducts cannot be reached,

and that eventually all the exo-adduct (173) would be converted to

the isomeric sultene (174). It is not known whether the

endo-adduct dissociates at these temperatures, nor whether a

1,3-dipolar cycloaddition[77] of the sulphine (148) to one double

bond of cyclopentadiene is involved as an alternative route to

(174).
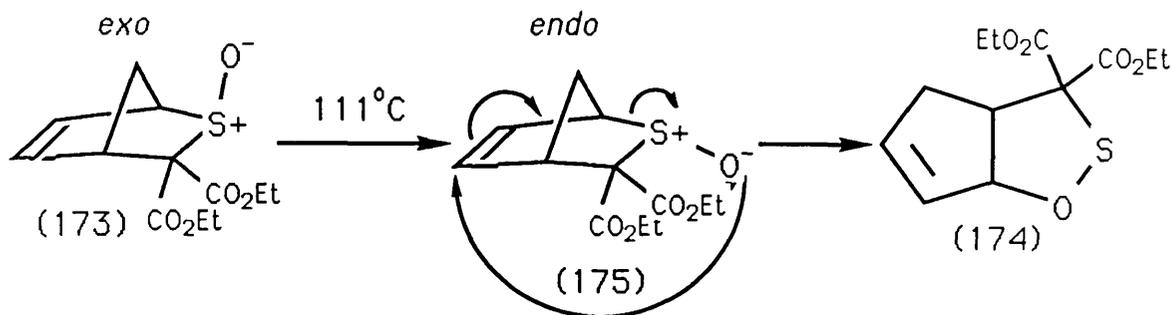
Scheme 61

(c) COMPETITION EXPERIMENT.

The anthracene adduct (172), cyclopentadiene (3 mol. equiv.) and

2,3-dimethyl-1,3-butadiene (3 mol. equiv.) were heated at 80°C in

refluxing benzene. This gave, after 1h, a mixture identical to

that of the transfer at 80°C, shown in Scheme 60. That is, a 2:1

mixture of (173) and (174) was produced. None of the 2,3-dimethyl-

-1,3-butadiene adduct (149) was detected, as expected since

cyclopentadiene is typically two orders of magnitude more reactive

than 2,3-dimethyl-1,3-butadiene [45] .

(d) FLASH VACUUM PYROLYSIS OF THE ANTHRACENE ADDUCT (172).
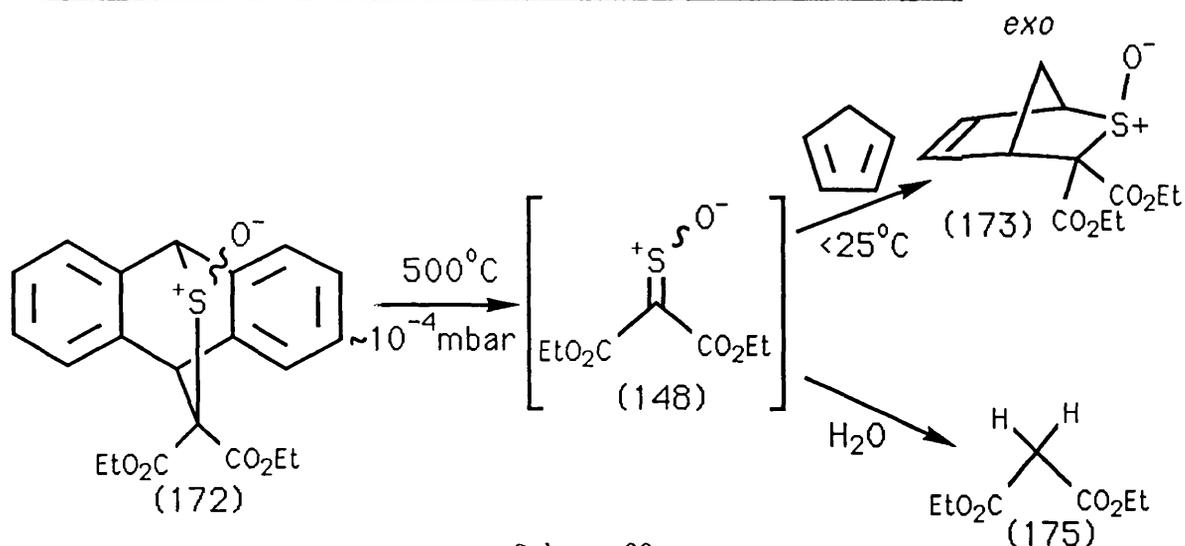
Scheme 62

The anthracene adduct (172) (1 mol. equiv.), deposited onto powdered, anhydrous magnesium sulphate by evaporation of a solution in dichloromethane, was sublimed under high vacuum (160°C at ca. 10^{-4} mbar) and allowed to pass through a quartz tube heated to 500°C. The adduct presumably dissociated in the hot tube, to give the sulphine (148) and anthracene. The latter was observed to solidify on the walls of the tube immediately after the oven, effectively separating it from the free sulphine (148), which was condensed in a cold trap (liquid-nitrogen temperature)

i) Reacting (148) with cyclopentadiene.

In the first experiment, cyclopentadiene (10 mol. equiv.) was condensed in the cold trap prior to generating the sulphine. Thus the sulphine was caught in the cold trap on a deposit of cyclopentadiene. The mixture was allowed to warm up to room temperature under a nitrogen atmosphere, and was dissolved in dichloromethane with more cyclopentadiene (10 mol. equiv.) for work-up. This experiment gave a mixture of products, the major product being the exo-cyclopentadiene adduct (173) in 47% yield. No endo-adduct was detected by ^{1}H n.m.r. ; however an unknown byproduct(s) was observed and will be discussed shortly (p90).

ii) Reacting (148) with water.

Water (20 mol. equiv.) was frozen in the cold trap prior to trapping of the sulphine. The mixture was dissolved in dichloromethane and worked-up to give diethyl malonate (175) as the major product, identifed by ^{1}H and ^{13}C n.m.r. spectroscopy, in a ratio of 3:2 with the byproduct(s) as in i) (ratio calculated from integration of the carboxyethyl signals in the 'H n.m.r.). No tetraethyl ethylenetetracarboxylate (155) was detected (using an authentic reference sample of (155)[74]). Elemental sulphur was, however, detected on t.l.c. This will be discussed shortly.

$$EtO_2C \quad\quad CO_2Et$$
$$EtO_2C \quad (155) \quad CO_2Et$$
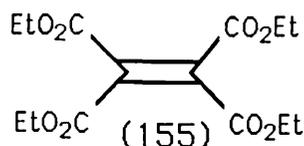
iii) Warming (148) to room temperature alone.

The sulphine (148) was caught in an empty, dry cold trap and allowed to warm to room temperature under a nitrogen atmosphere. This experiment gave some diethyl malonate (175) (from traces of moisture) and also the unknown byproduct(s) already mentioned in a ratio of 2:3 (calculated from integration of the carboxyethyl signals in the [1]H n.m.r.). Again no tetraethyl ethylenetetracarboxylate (155) was detected. Elemental sulphur was, however, detected on t.l.c.

Comments.

The observation that none of the endo-cyclopentadiene adduct (175) was detected, indicates a strong kinetic preference for exo addition of diethyl thioxomalonate S-oxide (148) to cyclopentadiene. This can be explained by addition of the sulphine

(148) to cyclopentadiene in the prefered conformation shown in
Scheme 63.   It is assumed that for a fast pericyclic reaction, the
sulphine group and one of the ester carbonyl groups should be
coplanar (for maximum overlap of p-orbitals).   Because of steric
repulsion between the sulphine oxygen and an ester group, the _trans_
ester carbonyl group will be coplanar with, and the _cis_ ester group
orthoganal to, the sulphine group.
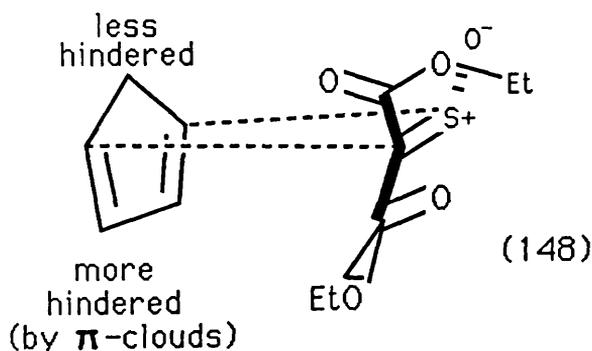
Scheme 63

The _trans_ ester group should then be _endo_ in the transition
state, as is usual in Diels-Alder reactions.   Moreover, _exo_
approach of the orthoganol ester group might be favoured on steric
grounds, since in general _exo_ cycloadducts are more stable
thermodynamically than the corresponding, kinetically favoured,
endo adducts.

However, the ratio of the exo- (173) and endo- (175)

cyclopentadiene adducts formed at 80°C in refluxing benzene was

ca.2:1 (the endo-adduct (175) was isolated as its rearrangement

product (174)). Also, the exo-adduct (173) was stable on

heating at this temperature. This means that the relative rates of

exo and endo cycloaddition must change with temperature (this is

true even if some of the endo-adduct (175) is converted into the

exo-isomer (173) before it can isomerise to the sultene (174)).

This would happen if the rate of endo addition changed more rapidly

with temperature than that of the exo addition. That is, if the

endo addition had the greater Arrhenius activation energy, E_a.

$$\ln k = -\frac{E_a}{RT} + \text{constant}$$

$$\therefore \frac{d \ln k}{dT} = \frac{E_a}{RT}$$

k = rate constant
E_a= activation energy
R = universal gas constant
T = temperature (K)

Table 4 : Some Mass Spectral Data for the Unknown Pyrolysis Product
Derived from the Sulphine (148).

measured $\underline{m/z}$	possible formula	calculated mass	possible structure
382.0751	$C_{14}H_{22}O_8S_2$	382.0805	(178)
380.0604	$C_{14}H_{20}O_8S_2$	380.0557	(176)
368.1134	$C_{14}H_{24}O_9S$	368.1205	(180)
350.1045	$C_{14}H_{22}O_8S$	350.0945	(179)
336.0284	$^{12}C_{12}{}^{13}CH_{15}O_7S_2$	336.0372	(177)

Less easily resolved is the structure of the aforementioned

byproduct(s) formed by flash vacuum pyrolysis of (172). This

pyrolysis product was presumably derived from the sulphine (148),

and was presumably polymeric. The ^{1}H n.m.r. spectra of the various

samples from these experiments showed only broad signals due to

ethoxycarbonyl groups. The ^{13}C n.m.r. spectra showed signals for an

ethoxycarbonyl group overlapping with those of diethyl malonate.

Any signals arising from quaternary carbons were too weak to be

positively identified (the sample was small). The high resolution EI

mass spectrum did, however, prove most informative (Table 4).

Scheme 64
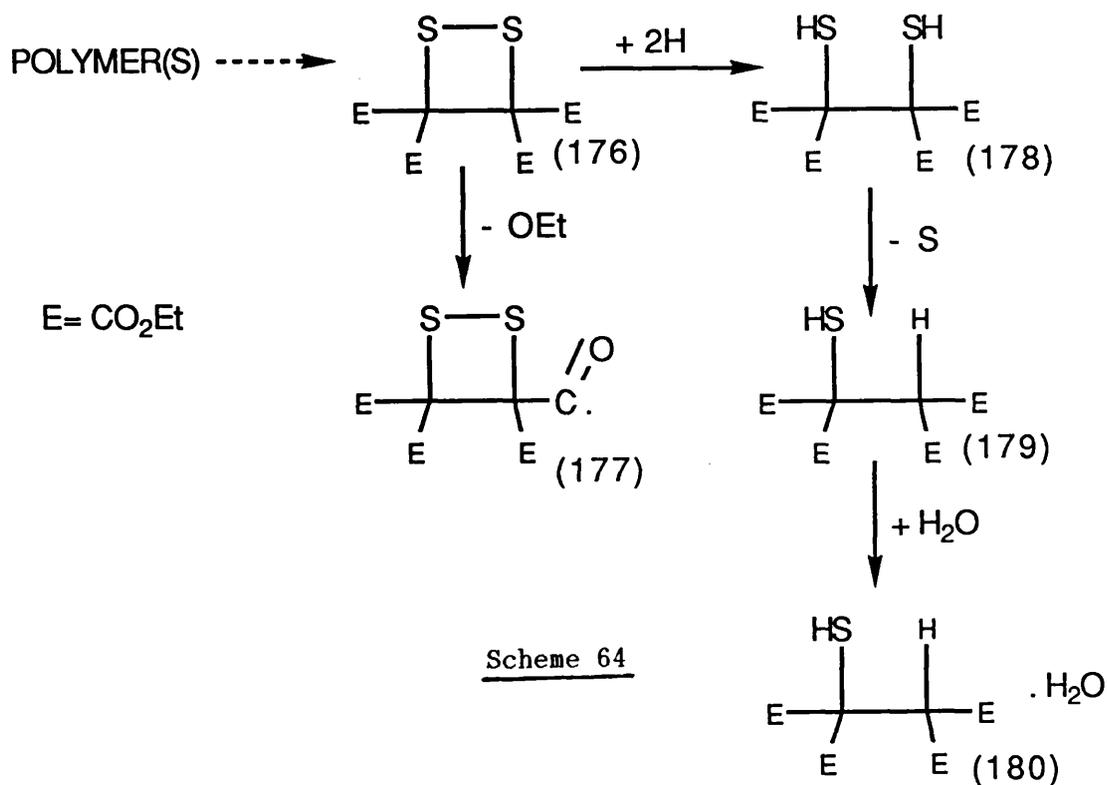
The mass spectral peaks in Table 4 are those of the highest $\underline{m}/\underline{z}$ values and it is suggested that they arise due to the decomposition of a polymer forming all or part of the unknown pyrolysis product(s) (a possible decomposition route is shown in Scheme 64). However, the detection of elemental sulphur on t.l.c. indicates that loss of sulphur has occured and it may be that the unknown product(s) are a mixture of oligomeric/polymeric material and decomposed oligomer/polymer. Note however that decomposition by the route suggested in Scheme 49 could not have taken place as no (155) was detected [74] .

Graph 3. Determination of rate constant (k) of dissociation of the anthracene adduct (172) of diethyl thioxomalonate S-oxide (148) at 60°C from the slope of $\ln(A-A_t)$ against time.

A = absorbance at 355nm at 24h.
A_t = absorbance at 355nm at time, t.

$k = 2.6 \times 10^{-4} \, s^{-1}$
$t_{\frac{1}{2}} = 44 \, min$

TIME (min)

(e) RATES OF DISSOCIATION OF THE ANTHRACENE ADDUCTS (127) AND (172).

xs.

60°C

(172) R= CO$_2$Et
(127) R=H   *trans*

(149) R= CO$_2$Et
(131) R= H   *trans*
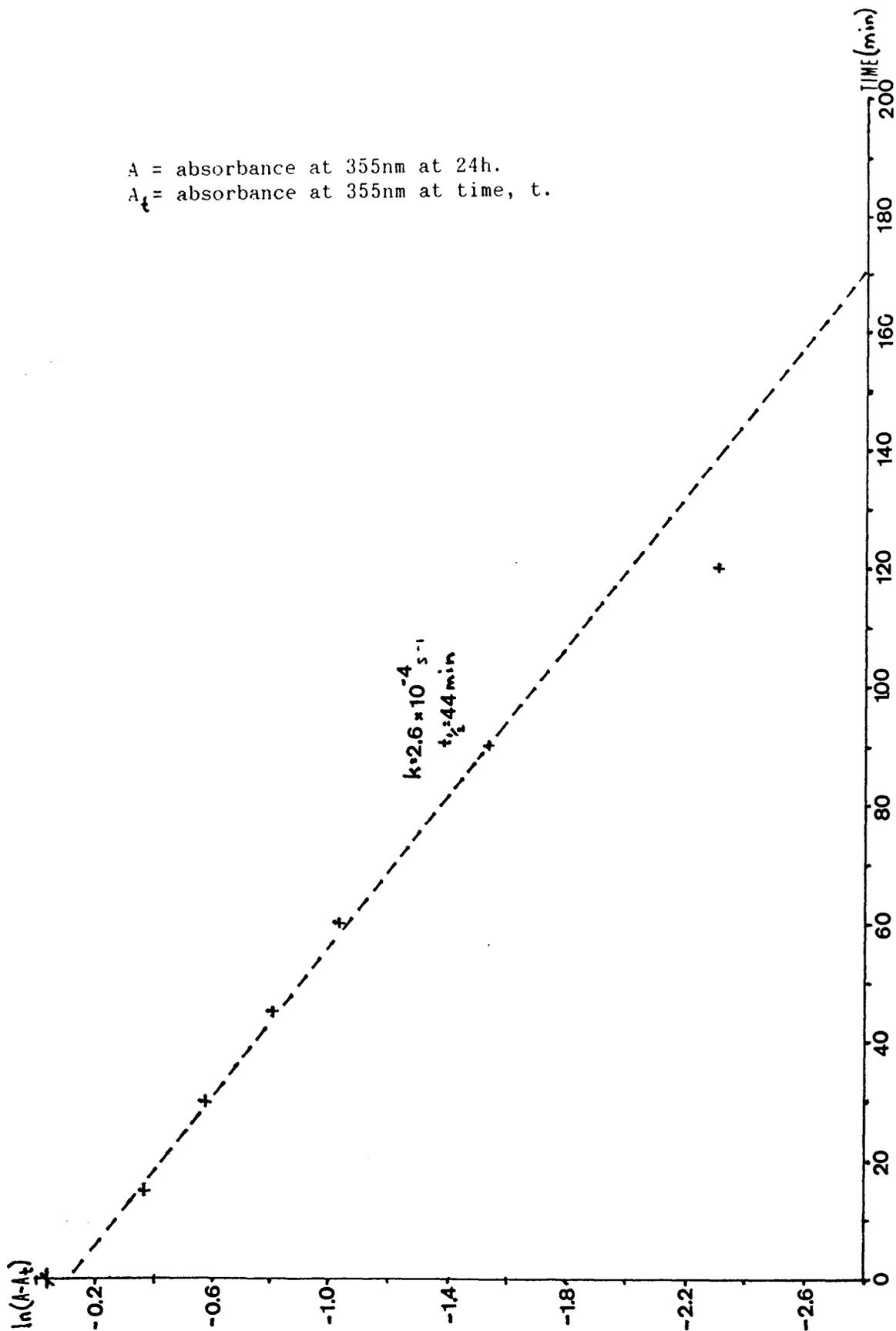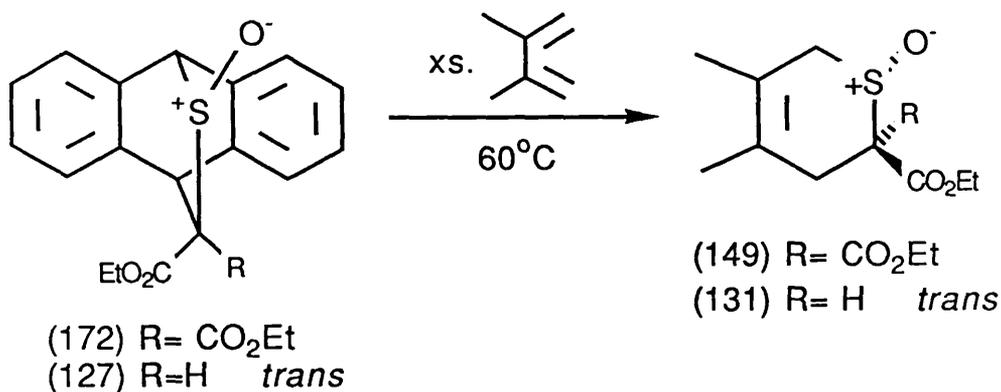
Scheme 65

The transfer reaction of the sulphine (148), generated at 80°C

from the anthracene adduct (172) and transferred to

2,3-dimethyl-1,3-butadiene to give (149) has already been discussed

(Scheme 59). This reaction was also studied at 60°C in benzene

using a tenfold excess of 2,3-dimethyl-1,3-butadiene (Scheme 65).

The kinetics of this reaction were measured (as for the

corresponding thione (46) transfer - p42) by following the increase

in an anthracene u.v. absorbance (355.0nm) with time at 60 ± 1°C,

in a water bath equipped with a thermostatic water heater and

mixer, and removing aliquots at specific time intervals. Thus the

reaction was shown to be approximately first order (Graph 3) with a

measured rate constant as shown in Table 5. This compares with

the rate of the corresponding "transfer" reaction of ethyl

thioxoacetate (E)-S-oxide (129) from anthracene to

2,3-dimethyl-1,3-butadiene at 60°C (Scheme 65) to give (131) which

was also shown [61] to be approximately first order . The latter

reaction was approximately half as fast as the former (Table 5).

This means the reaction is unimolecular (cf. p42) and also the

faster rate reflects the greater reactivity associated with two

electron-withdrawing groups on the sulphine (cf. p77).

Table 5.   Dissociation rates (k) of the anthracene adducts, (127)

and (172), of ethyl thioxoacetate (E)-S-oxide (129) and

diethyl thioxomalonate S-oxide (148), at 60°C in benzene.

Sulphine	k (s^{-1})	$t_{1/2}$ (min)
Ethyl thioxoacetate [a] (E)-S-oxide (129)	2.82×10^{-4}	41
Diethyl thioxomalonate S-oxide (148)	1.53×10^{-4}	76

Note

a   Using only 2 mol. equiv. of 2,3-dimethyl-1,3-butadiene.[61]

(f) REGIOSELECTIVITY OF DIELS-ALDER REACTIONS INVOLVING DIETHYL

THIOXOMALONATE S-OXIDE (148).
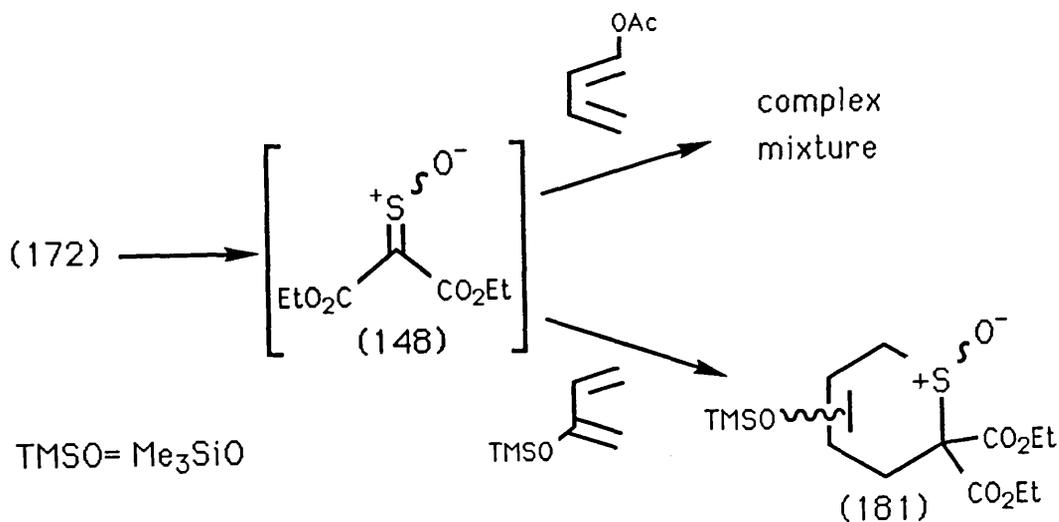
Scheme 66

The sulphine (148) was liberated in situ in refluxing benzene

from the anthracene adduct (172) and trapped in turn with

1-acetoxy-1,3-butadiene and then with

2-(trimethylsilyloxy)-1,3-butadiene (Scheme 66). The former diene

gave a mixture consisting of three or four components, which could

not be separated by t.l.c. and were not easily analysed by n.m.r.

spectroscopy. This reaction was abandoned as unnecessarily complex

for our purposes. The reaction of the sulphine (148) with

2-(trimethylsilyloxy)-1,3-butadiene (Scheme 66) proved much simpler

to study because, unlike the previous reaction with

1-acetoxy-1,3-butadiene, only one chiral centre can be produced.

The mixture of products (181) was easily hydrolysed[85] to give

stable ketones.

Reaction of Diethyl Thioxomalonate S-Oxide (148) with

2-(trimethylsilyloxy)-1,3-butadiene
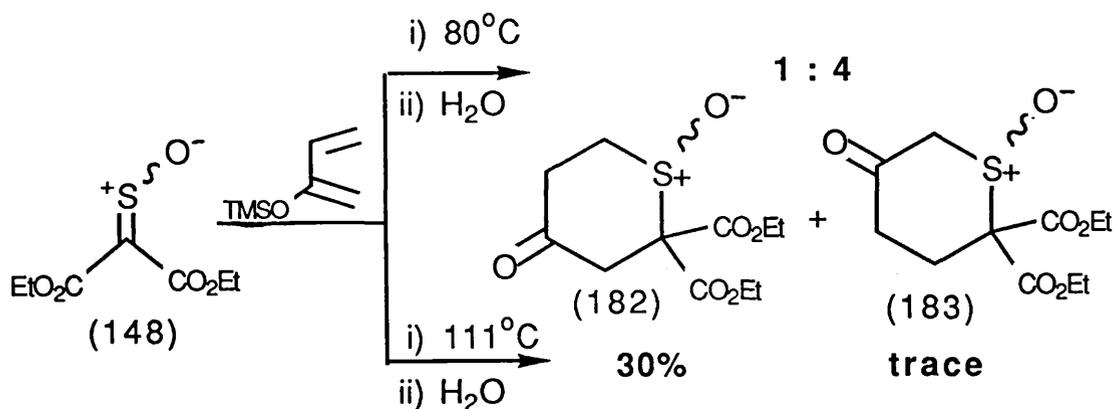
Scheme 67

i) in refluxing benzene (80°C).

The anthracene adduct (172) (1 mol. equiv.) was heated in

benzene under reflux, for 1h, in the presence of

2-(trimethylsilyloxy)-1,3-butadiene (2.5 mol. equiv.) under a

nitrogen atmosphere. The products were then hydrolysed[85] with

water and potassium fluoride in THF overnight to give a ca.1:4

mixture of the 4-oxo (182) and 5-oxo (183) regioisomers (in a

combined yield of 48%) as shown in Scheme 67. The mixture was

characterised by ^{1}H and ^{13}C n.m.r. spectroscopy, as will be

discussed shortly. The assignment of regiochemistry will also be

justified shortly.

ii) in refluxing toluene (111°C).

The anthracene adduct (172) (1 mol. equiv.) was heated in toluene under reflux, for 1h, in the presence of 2-(trimethylsilyloxy)-1,3-butadiene (3 mol. equiv.) under a nitrogen atmosphere. The products were then hydrolysed [85] with water and potassium fluoride in THF overnight to give the 4-oxo-regioisomer (182) in 30% yield as shown in Scheme 67. Only a trace of the 5-oxo-regioisomer (183) was detected by ^{1}H and ^{13}C n.m.r. spectroscopy.

Comments

The switchover in the major product when the temperature is changed from mainly (183) at 80°C to almost entirely (182) at 111°C can be explained in several ways. First, the rates of trapping of the sulphine (148) may show very different dependancies on temperature, that is the formation of each of the regioisomers have very different Arrhenius activation energies. Second, the adduct (183) could be labile, and redissociates to give (148) and the diene then reassociates to give (182). This requires (182) to be the thermodynamically more stable isomer. This second explanation is disfavoured, as non-bridged cycloadducts are not normally expected to undergo retro-Diels-Alder reaction as there is

no conformational strain to accelerate ring cleavage. A third

explanation is that the adduct (183) is largely decomposed at

111°C, but (182) is more stable. This is not considered likely in

view of the yield (30%) of (182) which is higher than would be

expected if this explanation were true.

It was hoped to distinguish between these explanations by

heating the 1:4 mixture of cycloadducts, formed initially in

refluxing benzene, in refluxing toluene to see if the ratio of

products changed. Unfortunately, when the mixture of cycloadducts

was heated in refluxing toluene for 1h, the resulting mixture was

complex. A second attempt also gave a complex product mixture,

possibly due to the presence of moisture in the reaction. Lack of

time prevented further research into this problem.

Table 6. ¹H and ¹³C n.m.r. data on the ketones (182) and (183). [δ(CDCl)]
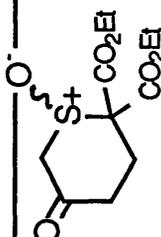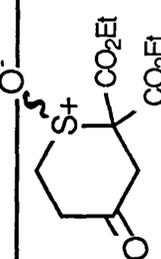
Compound / Nucleus		(183)		(182)	
¹H	3-H₂	2.50-3.22(m)	3-H₂	3.31(J 15.8Hz) 3.63(J 15.7Hz)	
	4-H₂		⨯		
	⨯		5-H₂	—	
	6-H₂	3.64(dd,H_eq J 14.5,1.3Hz) 4.09(d,H_ax J 14.4Hz)	6-H₂	2.38-3.20(m)	
¹³C	C-2	71.3	C-2	70.2	
	C-3	25.6	C-3	30.2	
	C-4	37.1	C-5	38.2	
	C-5	198.7	C-4	201.9	
	C-6	57.6	C-6	44.2	

Assignment of regiochemistry.

The sulphide (99) (1 mol. equiv.), which has been assigned

regiochemistry with the ketonic group in the 5-position (p45), was

oxidised with peracetic acid (1.2 mol equiv.) in diethyl ether at

room temperature, over 1h.   This gave diethyl 5-oxothiane

2,2-dicarboxylate S-oxide (183) quantitatively.   The spectra for

this oxidation product were identical to those for the major

component formed in refluxing benzene [i) p95].   This S-oxide

(183) is apparently "locked" into one conformation within the

n.m.r. timescale as we see no conformational averaging in the

^{1}H n.m.r. spectrum (Table 6), as described below.   The preferred

conformation (Scheme 68) is likely to have the S-O bond in the axial

position [86]   (183a) because of stereoelectronic effects

mechanistically related to the "gauche effect" [87] .

Scheme 68
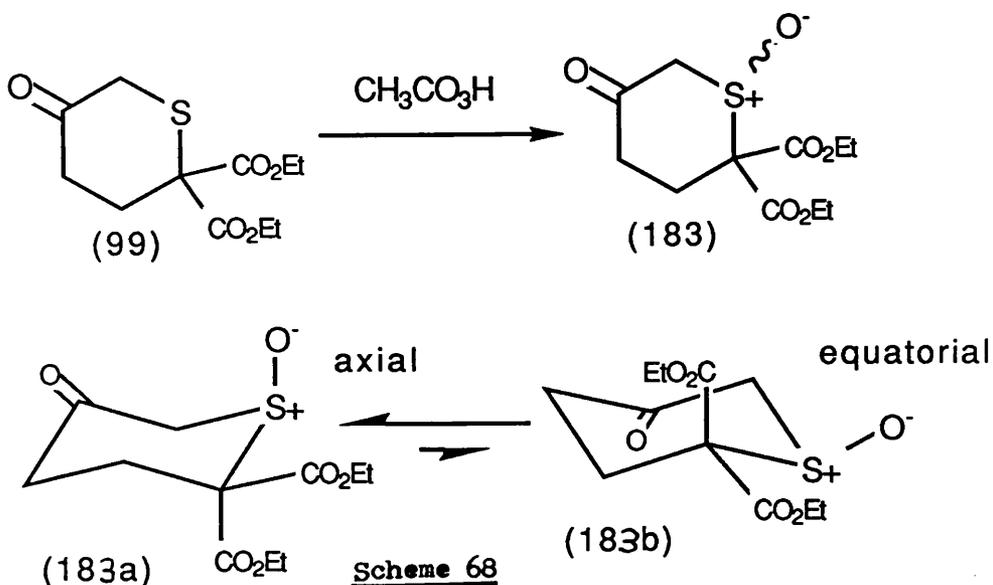
Figure 1. ^{1}H- ^{13}C direct shift correlation for (183). [δ (CDCl)]
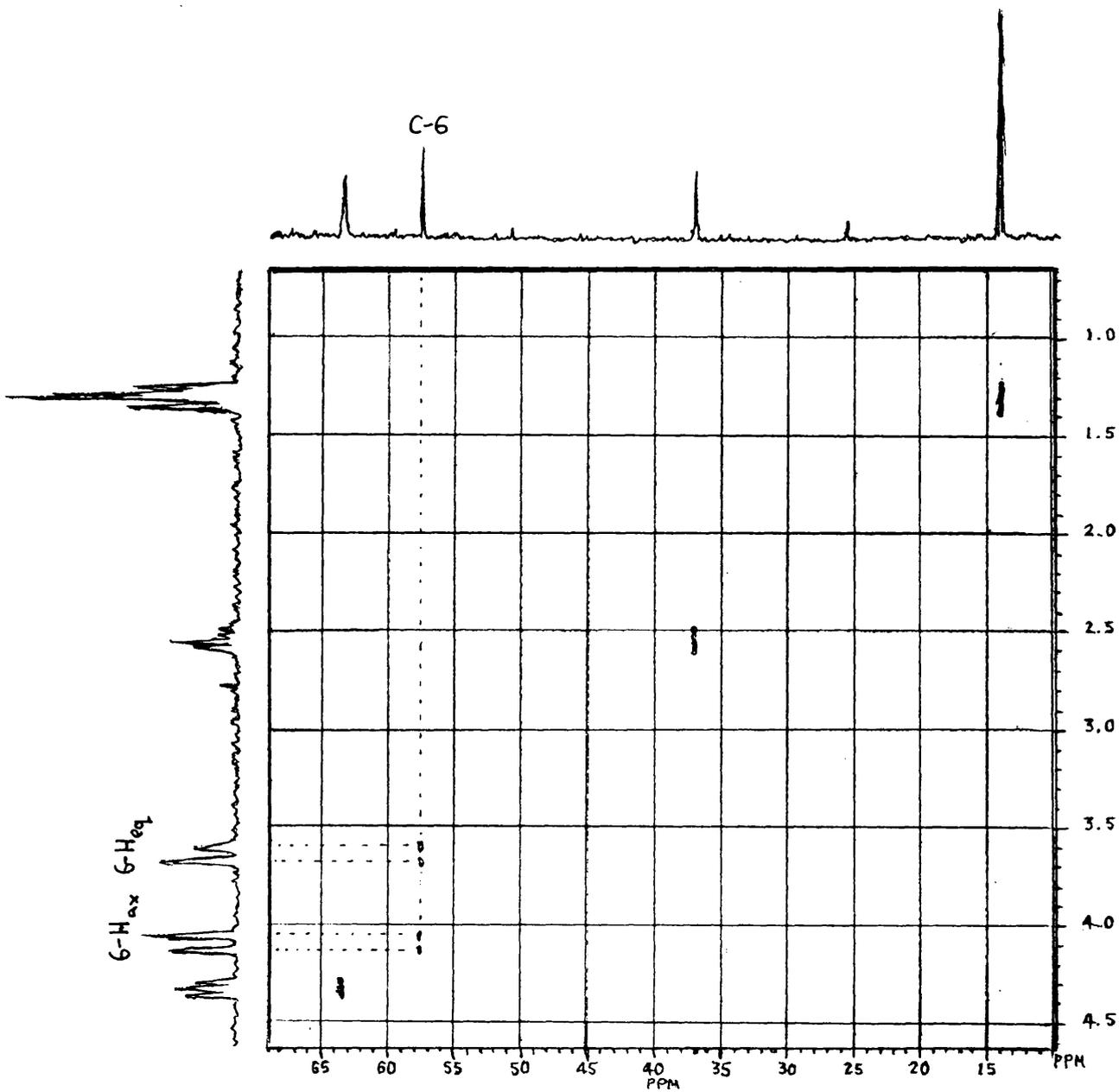
The ^{1}H n.m.r. and ^{13}C n.m.r. spectra of the ketone products

(182) and (183) alone are insufficient (Table 6) to justify saying

which represents the 4-oxo- and which the 5-oxo- regioisomer.

However, the structure (183) was unambiguously assigned to the

5-oxo-isomer (as has been assumed in preceding discussion) by ^{1}H-

^{13}C correlation n.m.r. (COSY) spectroscopy (Figure 1) on a sample of

(183) formed by oxidation of the corresponding sulphide (99) as

above.

The AB-quartets δ3.64 and 4.09 in one isomer and δ3.13 and 3.63

in the other must arise from isolated methylene groups (Table 6).

To decide which AB-quartet arises from an isolated 3-H$_2$ and which

from an isolated 6-H$_2$, we must correlate them to the appropriate

carbon nucleus. Firstly, we must know which carbon signal is C-6

in the sample obtained by oxidation of (99). This was assigned by

comparison with the spectra for the sulphide (47) and its $\underline{S}$-oxide

(149). These have their C-6 signals at δ37.7 and 50.6 respectively

and C-3 signals at δ30.8 and 27.7 respectively. Thus the highly

deshielded signal at δ57.6 is assigned to C-6 of the oxidation

product. Once this was realised, a COSY experiment (Figure 1)

showed that the C-6 signal at δ57.6 was directly coupled (one-bond

coupling) to the methylene group at δ3.64 and 4.09, which as it is

a simple AB-quartet, means that the 6-methylene group is adjacent

to the ketonic group; that is, this sample is the 5-oxo-isomer

(183). This unambiguously assigned the regiochemistry of the

preceeding reactions. Also, as expected for a compound having a

single,predominant conformation (183a) or (183b), a W-coupling

(1.3Hz) was observed between the equatorial hydrogens on C-6 and

C-4.

CONCLUSIONS.

The anthracene adduct (172) and, to a lesser extent, the exo-cyclopentadiene adduct (173), of diethyl thioxomalonate S-oxide (148) are useful auxiliary precursors, liberating the electrophilic sulphine (148) on heating. This sulphine can then be 'transferred' to other dienes. The endo-cyclopentadiene adduct (175) was not detected and presumably rearranges rapidly to the stable sultene (174). Flash vacuum pyrolysis of the anthracene adduct (172) is a good method of generating the free sulphine (148), but this method is limited by the susceptibility of (148) to rapid hydrolysis and oligomerisation/polymerisation. The regiochemistry of cycloaddition of the sulphine (148) was also studied and the product ratios shown to be temperature dependent.

CHAPTER 3

"THE SYNTHESIS AND REACTIONS OF DIETHYL SELENOXOMALONATE."

INTRODUCTION

STABILITY OF SELENOCARBONYL GROUP.

Studies of the chemistry of selenocarbonyl compounds have been rather limited and reviews are sparse[88-92]. Due to poor orbital overlap and different spacial symmetry, the $(2p-4p)$ π-bond in such compounds is expected to be less stable than the π-bond in corresponding thiocarbonyl compounds, and much less stable than in carbonyl compounds. However, calculations based on ^{77}Se and ^{17}O n.m.r. data on stable selenoketones (selones) and on ketones indicate that the bond order of selenocarbonyl and carbonyl groups are comparable[93], and that selenocarbonyl groups are genuinely C-Se doubly bonded.

Although the C-Se π-bond is extremely reactive (most reactions
involve the ready interconversion of the C-Se double bond into a
single bond), there are examples of selenocarbonyl compounds
stabilised by resonance; so that selenoamides[94-96](184) are isolable
compounds.

$$
\underset{\displaystyle \text{(184)}}{
R^1\text{—}\overset{\displaystyle Se}{C}\text{—}NR^2R^3
\quad\longleftrightarrow\quad
R^1\text{—}\overset{\displaystyle \overset{-}{Se}}{C}\text{=}\overset{+}{N}R^2R^3
}
$$
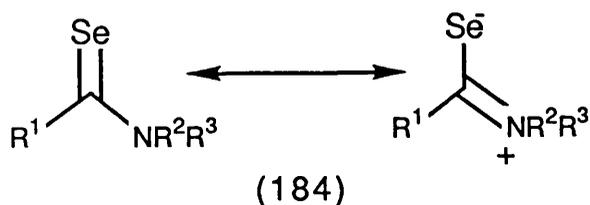
In contrast, with electron-withdrawing substituents in the
α-position, selenocarbonyl compounds become even more reactive,
because the energy of the carbon 2p orbital is reduced.   These
unstable selenocarbonyl compounds include those with attached
ketonic[97-99]   (185), ester [97-100]   (186), p-nitrophenyl[97,99,100]
(187), and cyano [97,99]   (188) groups.

$$
R^1\text{—}\overset{\displaystyle Se}{C}\text{—}Z
$$

(185) Z=COR^2
(186) Z=CO$_2$R^2
(187) Z= p-NO$_2$C$_6$H$_4$
(188) Z= CN
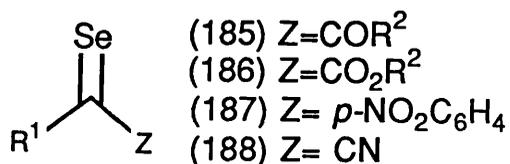
An alternative source of stability in selenoketones is found in sterically congested molecules, for example (189)[101] and (190)[101,102], both of which are stable and blue (due to n→ π* transitions). However, in the presence of oxygen and light, sterically hindered selones precipitate elemental selenium and give the corresponding ketone[101].
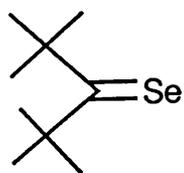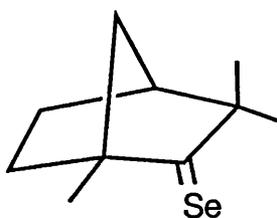
(189)   (190)

THE DISCOVERY AND SYNTHESIS OF SELENOKETONES.

The earliest reactions which produced selenoketones gave dimers

of the selone [102,103]. In an earlier example [93], treatment of

benzaldehyde (191) with hydrogen selenide (Scheme 69) gave,

presumably, selenobenzaldehyde (192) which underwent both reduction

by the excess of hydrogen selenide to give the selenol (194), which

oxidises in air to the diselenide (195), and simultaneous

trimerisation to give (196), presumably as a mixture of

stereoisomers.

(191) R=Ph   (192) R=Ph   (196) R=Ph
(10) R=H   (193) R=H   (197) R=H
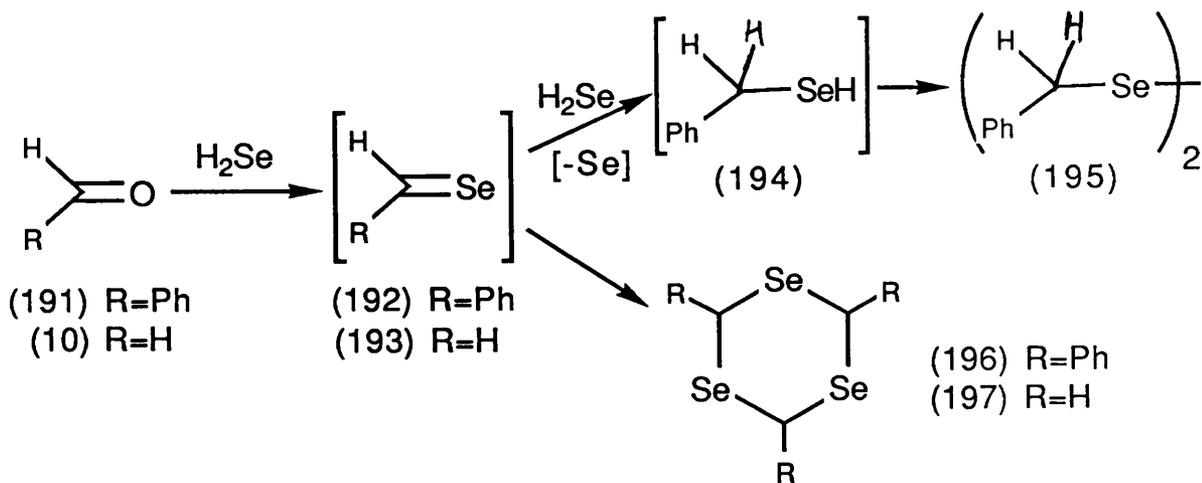
Scheme 69

Similar treatment[94]   of (unhindered) formaldehyde (10) with

hydrogen selenide gave only the trimer (197), presumably via

selenoformaldehyde (193) (Scheme 69).

The earliest well-documented formation of a selenoketone[101]

involved treating the phosphoranylidene hydrazone (198) with

selenium powder at 120°C to give the sterically hindered,

di-t-butyl selone (189) (Scheme 70).

(189)   **(189)**
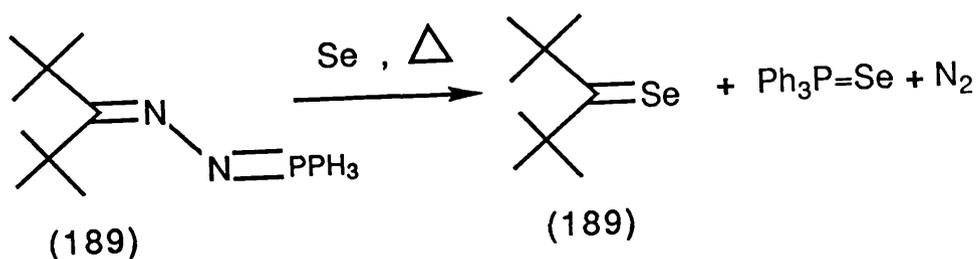
Scheme 70

Of these methods hydrogen selenide has proven to be somewhat too

unpleasant and toxic to use[92,104], and has had little successful

application to the synthesis of selenoketones, often acting as a

reducing agent to give diselenides[103] .

Phosphorus pentaselenide has also been of limited utility in selone synthesis [92,105], often decomposing with moisture to give

hydrogen selenide gas. Conflicting evidence surrounds its [96,106-108]

structure and even its colour. It is generally prepared by heating

gray selenium and red phosphorus at high temperatures [96,108], but

often is generated _in situ_ in reactions to form selones [94]. A good

example of its successful use was provided by Rae and Wade [95] in

1976. They heated various amides with phosphorus pentaselenide and

barium carbonate in refluxing xylene for 24h; for example (199)

gave the selenoamide (200) in 61% yield (Scheme 71).
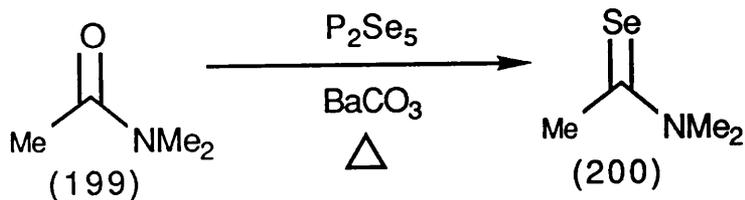
Scheme 71

Replacement of sulphur by selenium seems to be more favourable

(because of the reactivity of thiocarbonyl groups) and Mickey and

Zingaro [96] showed that 1-alkyl-4-thiouracils (201) could be

selenated by heating with phosphorus pentaselenide in refluxing

pyridine for 24h to give (202), but in very low yields (Scheme

72).
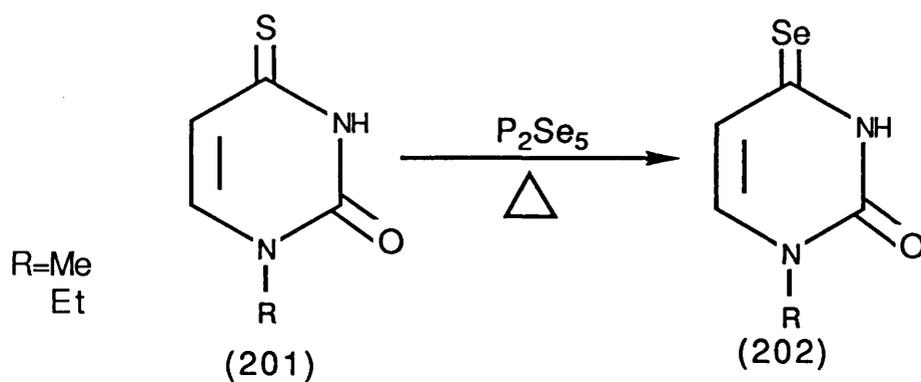
Scheme 72

The reported yields of such reactions of phosphorus pentaselenide

vary from good to poor; this may be attributed to the variable

quality of this reagent which, it seems cannot be recrystallised.[107,108]

Many of the other methods of preparing selones (206) involve

directly treating species such as (203), (204) or (205) with

elemental selenium (Scheme 73).

(203) X=PPh₃ [100]
(204) X=NNPPh₃ [101]
(205) X=SMe₂ [98]
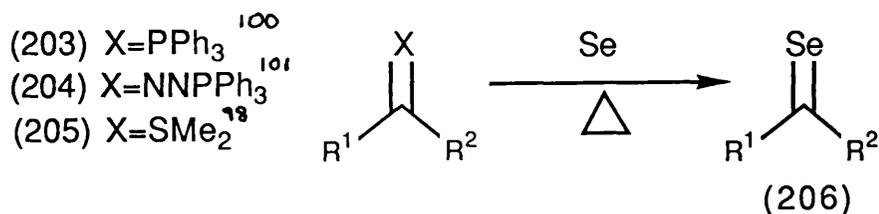
Scheme 73

Similarly, the hydrazone derivative (207) has been used[109,110] for

the synthesis of sterically hindered selones such as (190) by

treatment with selenium halides (Scheme 74). However this method

has not been successfully extended to the synthesis of more

reactive selones.
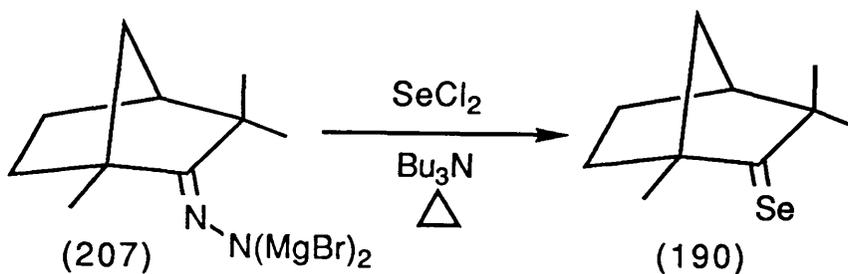
Scheme 74

For completeness, the first report of the synthesis of a transient telluroaldehyde deserves inclusion [111]. Treatment with a phosponium ylid (208) with elemental tellurium at 105°C. gave tellurobenzaldehyde (209) which was trapped <u>in situ</u> with 2,3-dimethyl-1,3-butadiene to give the moisture-sensitive cycloadduct (210) in 11% yield (Scheme 75). This cycloadduct was characterised by mass spectroscopy and n.m.r. spectroscopy, the spectra being compared with the corresponding selenium and sulphur derivatives.
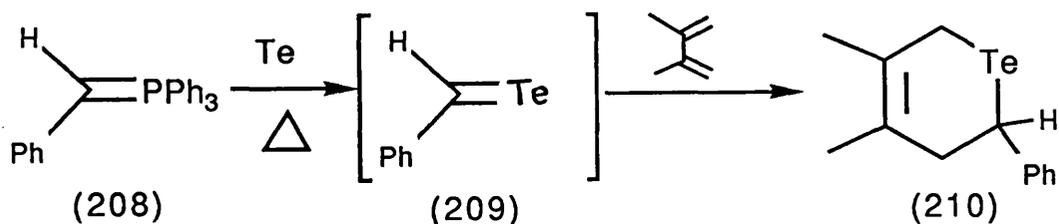
<center>Scheme 75</center>

Recently, good reagents for the direct selenation of ketones

have been developed (Scheme 76). They are bis(tricyclohexyltin)

selenide[101,112], which selenated fenchone (211) to give

selenofenchone (212) in 90% yield, and bis(trimethylsilyl)

selenide,[113] which gave a variety of unstable selenoaldehydes (214)

which were trapped *in situ* with cyclopentadiene to give the

cycloadducts (215) in *ca*. 70% yield.
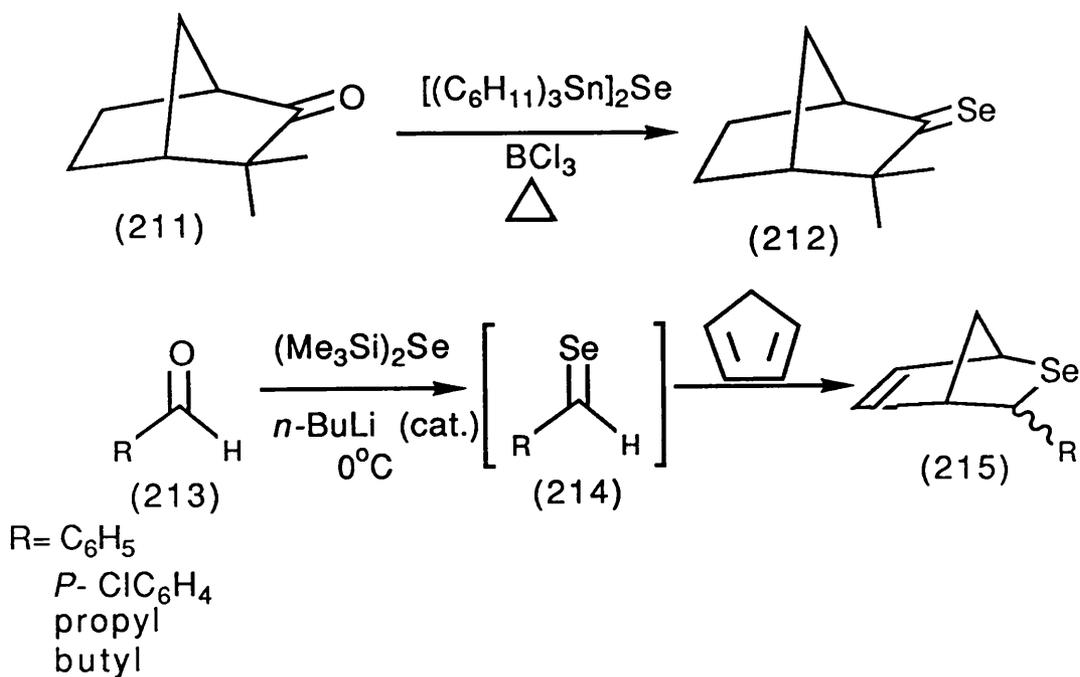
Scheme 76

GENERATION OF SELENOCARBONYL COMPOUNDS BY RETRO-DIELS-ALDER REACTION

To date, the only generation of selenoaldehydes by the

retro-Diels-Alder reaction has been by Kirby and Tretheway[99]

(there have been no reports of selenoketones being generated in

retro-Diels-Alder reactions). They prepared anthracene,

9,10-dimethylanthracene and cyclopentadiene adducts of various

selenoaldhydes, formed in situ by elimination of HX from selenenyl

derivatives, ZCH_2SeX (Scheme 78). They found that the anthracene

adducts (216) dissociated on heating to give the selenoaldehydes

(217) which were trapped in situ with 2,3-dimethyl-1,3-butadiene to

give adducts (218) in high yields (Scheme 77). Also the

cyclopentadiene adducts (219), as a 1:1 mixture of endo- and

exo-isomers, dissociated thermally to give the selenoaldehydes

(220) which again were trapped to give the adducts (221) in high

yield. Generally the α- substituents, Z in ZCHSe, were

electron-withdrawing.
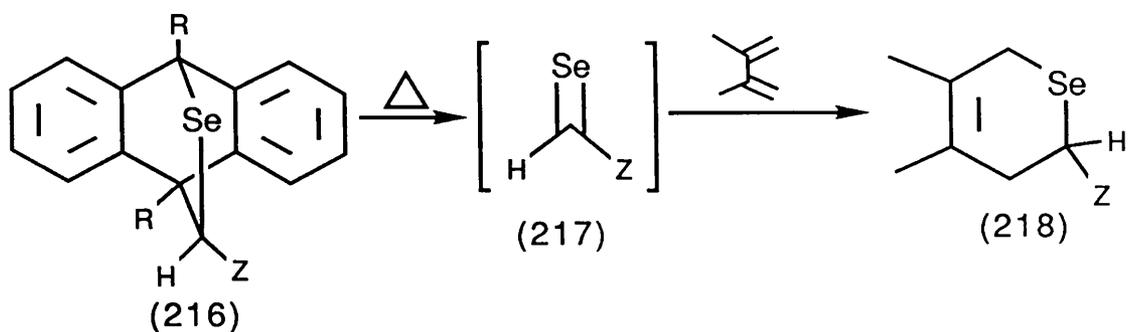
R= H or Me ; Z=CO$_2$Et
R=Me ; Z= COPh, CN

Z= EtO$_2$C
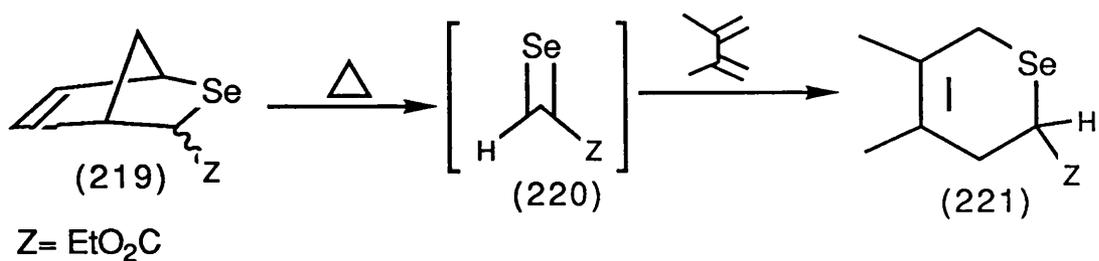
Scheme 77

α-OXOSELENOCARBONYL COMPOUNDS.

α-Oxoselenoaldehydes (223) have been generated (Scheme 78) by elimination of HX from appropriate selenenyl compounds[97,99] (222). The selenoaldehydes (223) were then trapped <u>in situ</u> with a suitable diene, <u>eg</u>. cyclopentadiene to give (224), in moderate yields.
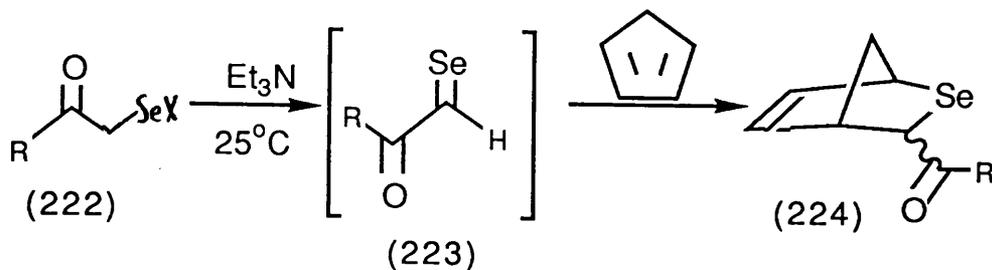
Scheme 78

A route to α-oxoselenoketones has also appeared in the literature [98]. This involves the reaction of a dimethyl sulphonium ylid (225) with elemental selenium in refluxing <u>o</u>-dichlorobenzene (Scheme 79). The first formed selenoketone (226) was then trapped with a suitable diene, <u>eg</u>. 2,3-dimethyl-1,3-butadiene, to give stable adducts (227) in moderate to high yields.
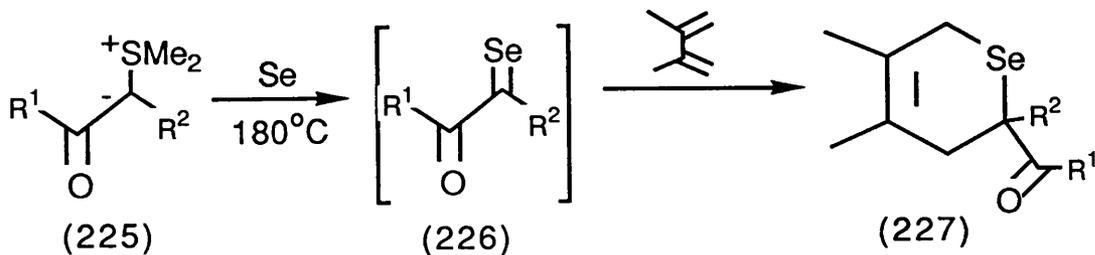
Scheme 79

SELENOXOMALONATES.

The method shown in Scheme 80 for the synthesis of

α-oxoselenocarbonyl compounds was applied [98] , after our own

studies had commenced, to the synthesis of diethyl selenoxomalonate

(229). Heating the ylid[114] (228) in o-dichlorobenzene under reflux

with elemental selenium generated the corresponding selone (229)

which was trapped with cyclopentadiene (formed in situ from

dicyclopentadiene), to give the cycloadduct (230) in 78% yield

(Scheme 80). Remarkably, this product survived the prolonged

heating at ca. 180°C.
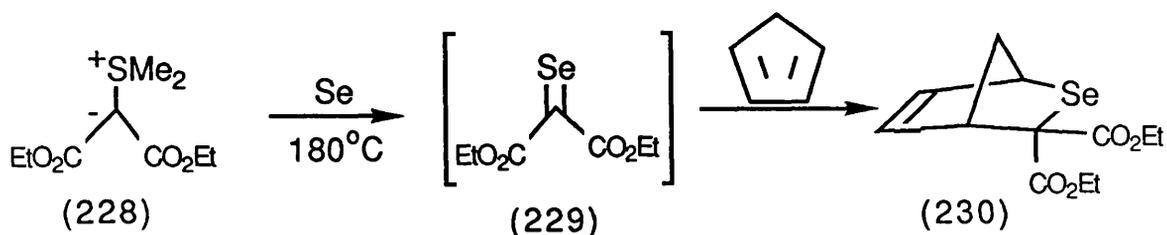
Scheme 80

REACTIONS OF THE SELENOCARBONYL GROUP.

Studies of the reactions of selenocarbonyl compounds have been mostly conducted on stable selenoketones[92] . Some similarities are shown to the chemistry of thiocarbonyl compounds, in that most of the reactions centre around the instability of the C-Se π-bond. Thus the primary difference between seleno- and thio-carbonyl compounds is that selenocarbonyl compounds generally react faster.

For example, in an analogous manner to thiocarbonyl and carbonyl compounds, selones (206) can be quantitatively reduced[101] (Scheme 81) with sodium borohydride to selenols (231) which are air-sensitive and so give stable diselenides (232) upon work-up.
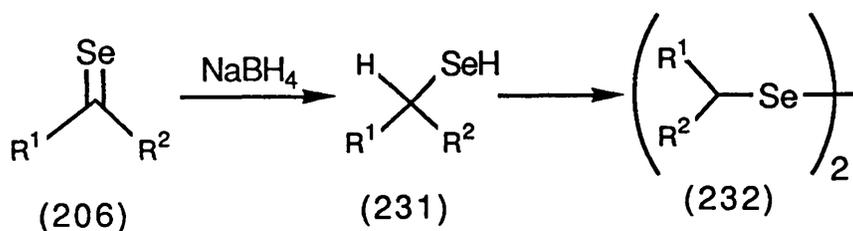
Scheme 81

Treatment of selones (206) with a slight excess of sulphur[115] or

phosphorus pentasulphide [116] generally gives the corresponding

thiones (54) in good yield (Scheme 82).
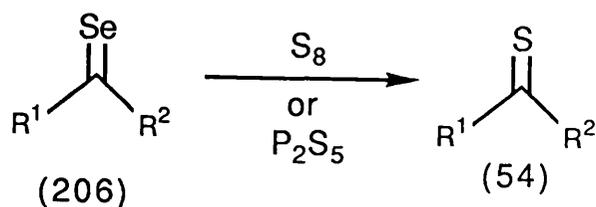
Scheme 82

(a)   REACTIONS OF SELENOKETONES WITH NUCLEOPHILES.

Sterically hindered selones react with organometallic compounds,
often giving selenols (which oxidise in air to diselenides)[92] as
well as undergoing "selenophilic" addition. Di-t-butyl selone
(189) reacts [92] with phenyl lithium to give only the
"selenophilic" addition product (233), whereas the corresponding
thione (114) gives a mixture[117] of thiophilic, to give (234), and
carbophilic, to give (235), addition (Scheme 83).
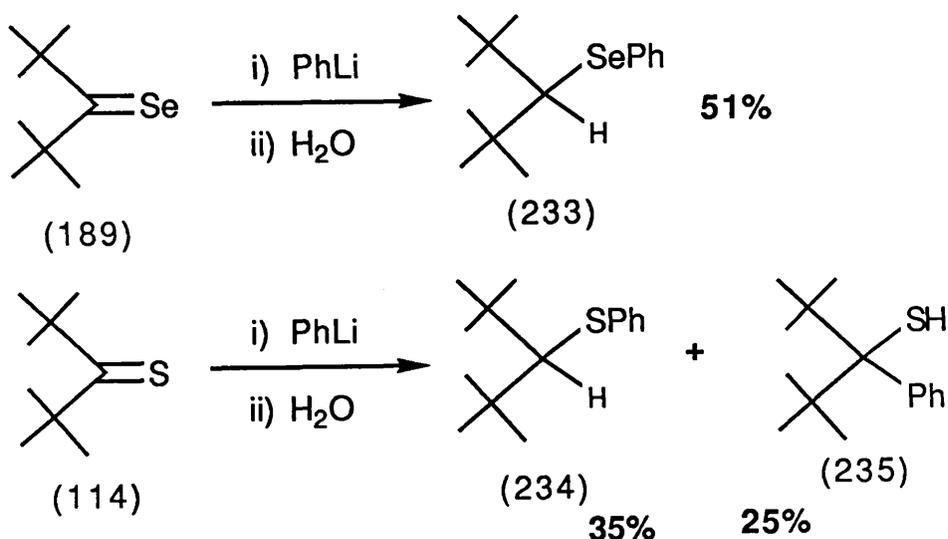
Scheme 83

(b)   REACTIONS OF SELENOCARBONYL COMPOUNDS WITH CONJUGATED DIENES.

Transient selenoaldehydes and selenoketones have been studied by

generating them as reactive intermediates, and then trapping them
                                         97-101,109
in situ with conjugated dienes   , such as cyclopentadiene.

Regiochemistry of Diels-Alder Reactions.

Meinke and Krafft [97] studied the reactions of a variety of

reactive selonoaldehydes with asymmetric dienes. For example, they

showed that the selenoaldehyde (237), generated in situ from the

selenocyanate (236), reacted with 2-ethoxy-1,3-butadiene to give a

19:1 mixture of regioisomers (238) and (239) in 75% yield (Scheme

84).
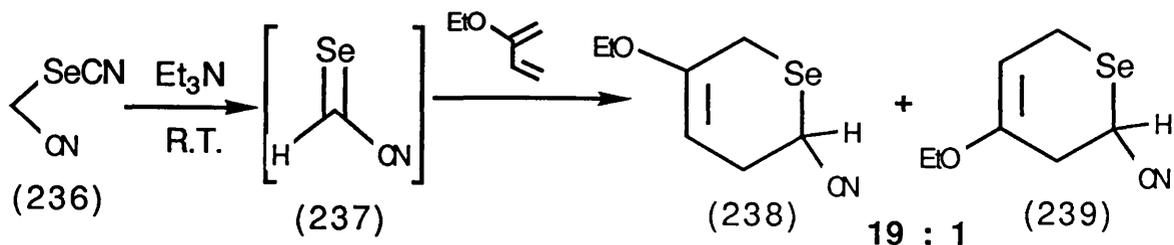
Scheme 84

They suggest that the major route of such reactions should be
controlled by the HOMO of the diene and the LUMO of the
selenoaldehyde, as shown in Scheme 85.   The presence of an
electron-donating   group(s) on the diene will accelerate the
reaction and increase its regioselectivity.

X= electron-donating group
Z=electron-withdrawing group

major   *minor*
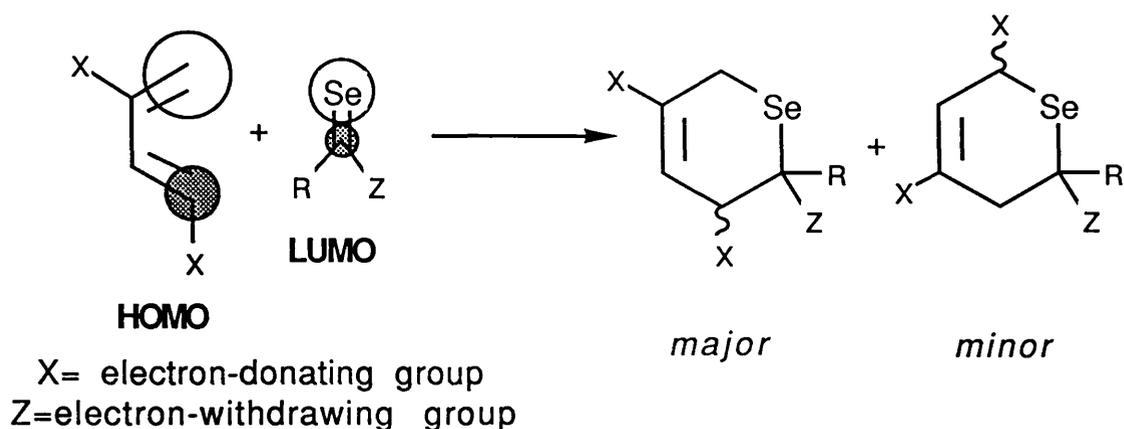
Scheme 85

An example of this kind of regioselectivity was demonstrated
(Scheme 86) by Kirby and Tretheway [99] who generated ethyl
selenoxoacetate (220) from the selenosulphate (240).   The
selenoaldehyde (220) was trapped with thebaine (40) to give
regiospecifically a ca. 1:1 mixture of the epimeric endo and exo
adducts (241).
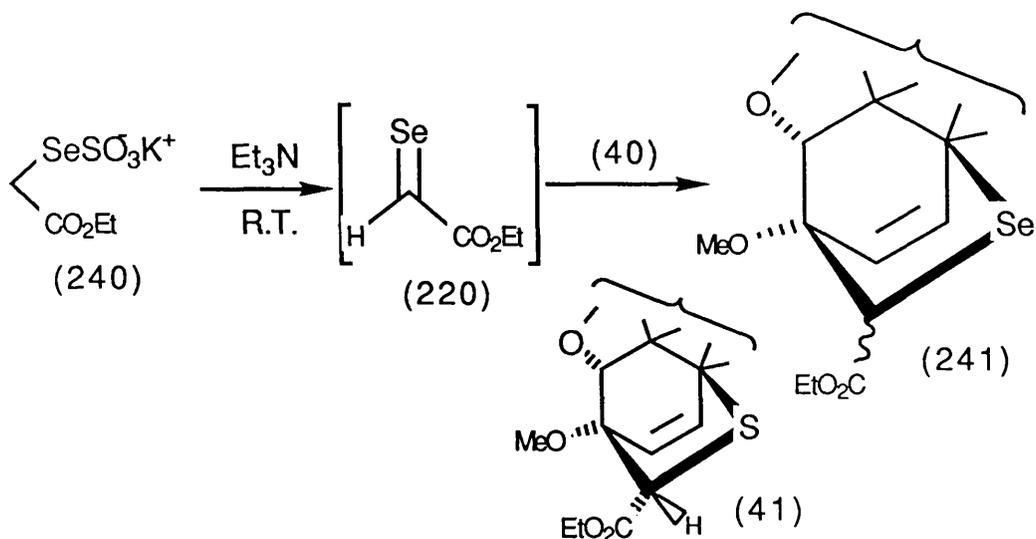
Scheme 86

Ethyl thioxoacetate (28) added to thebaine highly regioselectively

in the same sense (Scheme 10) to give very largely the endo epimer

(41). A similar reduction in stereoselectivity of ethyl

selenoxoacetate (220) compared with ethyl thioxoacetate (28) was

observed in their cycloaddition to cyclopentadiene and

cyclohexadiene [99] . It was suggested that the selenium compound

was more reactive and this led to cycloaddition via an "earlier",

more reactant-like transition state resulting in smaller secondary

orbital interactions. The longer C-Se bond length may also be a

contributing factor.

(c)   OXIDATION OF SELONES.

Oxidation of di-t-butyl selone (189) with m-chloroperoxybenzoic

acid (mCPBA) at low temperature gave, presumably, the selenine

(242) which however decomposed at -20°C to give the ketone (243)

and elemental selenium [101,118] (Scheme 87). This is the only

report of a selenine in the chemical literature. This contrasts

sharply with the known stability of the sulphur analogue [63,64]

(115) formed in Scheme 37.
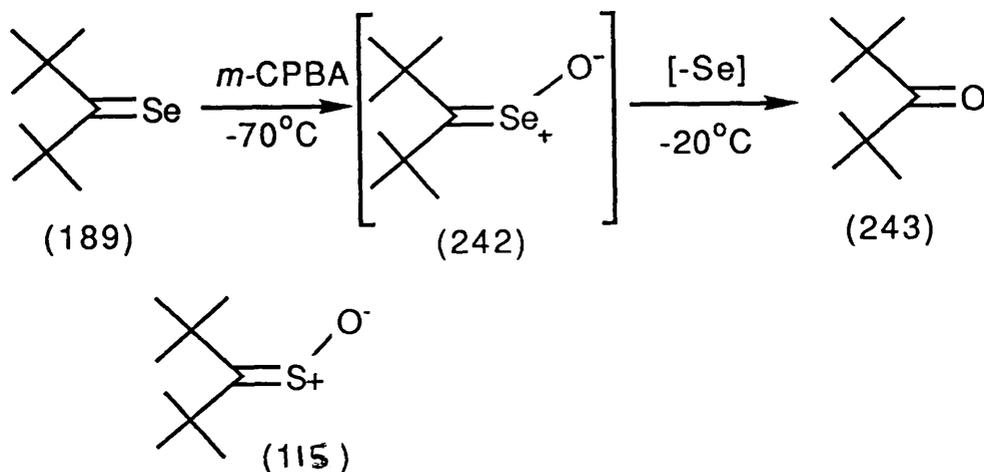
Scheme 87

DISCUSSION

SYNTHESIS OF DIETHYL SELENOXOMALONATE (229).

Diethyl selenoxomalonate (229) has only appeared once in the chemical literature [98] and remains more difficult to make than its sulphur counterpart. It is expected to be less stable than the corresponding thioketone (46) because the π-bond is formed by overlap between the selenium 4p and carbon 2p orbitals, which gives a genuine π-bond [93] , although the gross mismatch in size and energy of the p-orbitals make it highly reactive.

$$\underset{\text{EtO}_2\text{C}}{}\overset{\text{Se}}{\underset{}{\|}}\underset{\text{CO}_2\text{Et}}{}$$

(229)
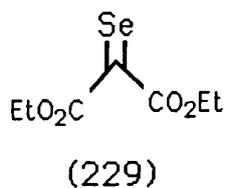
The cyclopentadiene and anthracene cycloadducts of (229) were considered to be potentially useful auxilliary precursors for this selone, presumably liberating (229) on heating by retro-Diels-Alder reaction. So some synthetic approaches to these adducts were explored.

(a)   APPROACHES FROM PHOSPHORUS PENTASELENIDE.

Because of the contradictory reports regarding the quality and
nature of phosphorus pentaselenide, and its tendency to decompose
to hydrogen selenide gas, it was considered preferable to attempt
to generate it <u>in situ</u> [94]   .

Treatment of diethyl oxomalonate (48) (1 mol. equiv.) with
intimately ground red phosphorus (1 mol. equiv.), gray selenium (1
mol. equiv.), and barium carbonate (1 mol. equiv.) in dry pyridine,
in the presence of cyclopentadiene (5 mol. equiv.), at reflux over
24h, in a nitrogen atmosphere, gave only quantitative recovery of
the starting ketone (48). When <u>o</u>-dichlorobenzene (b.pt. 180°C) was
used instead of pyridine, the same negative result was obtained.
Similarly, <u>N</u>-methyl pyrrolidin-2-one [95]   could not be selenated
under equivalent conditions.

(b)   APPROACHES FROM DIETHYL SELENOCYANATE (244).

It was known at the start of this investigation[119] that diethyl

selenocyanatomalonate (244) could be made from diethyl

bromomalonate (91), by treatment with potassium selonocyanate in

refluxing ethanol (Scheme 88).
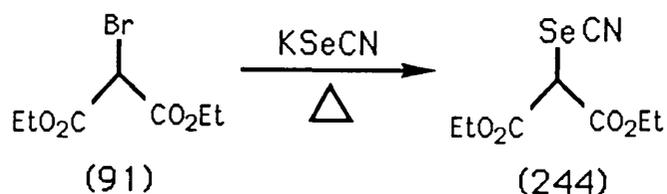
Scheme 88

It was also known that treatment of this selenocyanate (244) with

triethylamine, in ethanol containing calcium chloride (to remove

cyanide ions by precipitation), at room temperature in the presence

of cyclopentadiene gave, unexpectedly, the cyclopropyl compound

(248). Two mechanisms were considered for this reaction (Scheme

89). The first involved generation of a carbene (245) and

cheletropic addition to one double bond of the diene (Path A). The

second involved generation of the selenoketone (229), trapping in

situ to give the desired cycloadduct (230), and subsequent

rearrangement with loss of elemental selenium to give the

cyclopropane (248) either thermally (Path B) or catalysed by

base (Path C). However the recent preparation of the

cyclopentadiene adduct (230) demonstrates its high thermal

stability [98] , even at 180°C. Addition of a radical inhibitor

to, and exclusion of light from, the reaction mixture had no effect

on the outcome.
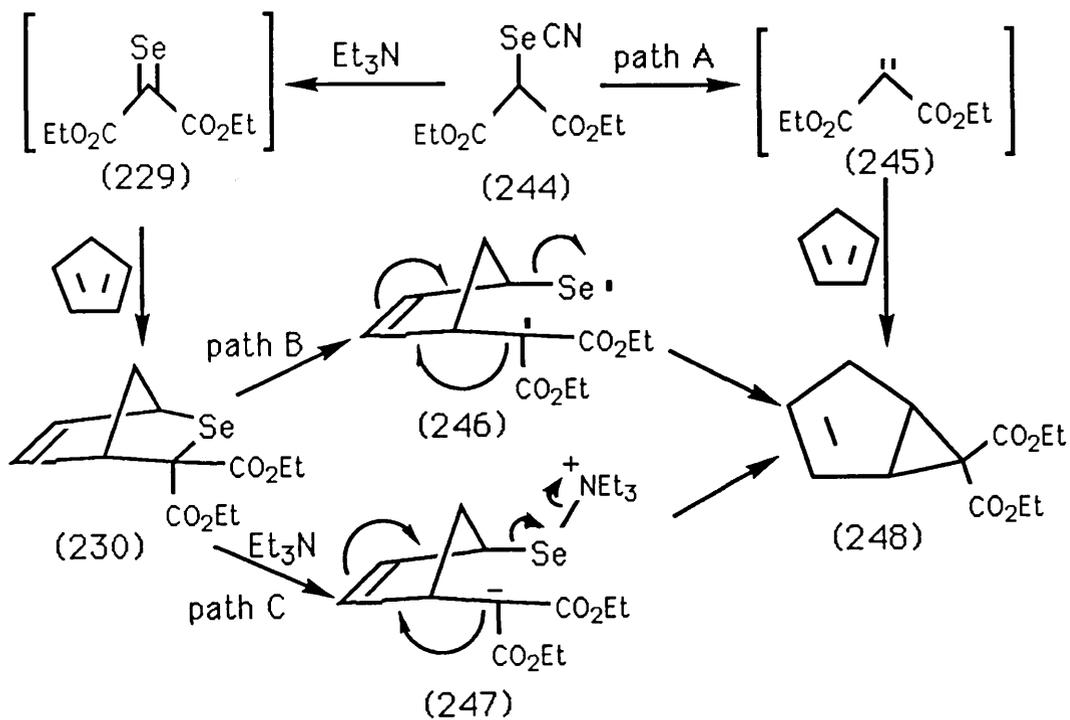
Scheme 89

To extend these preliminary findings, the selenocyanate (244)

was prepared, as before, from diethyl bromomalonate and potassium

selenocyanate in refluxing ethanol over 1h. It was found that

diethyl malonate was always formed as a byproduct, the

selenocyanate being separated by fractional distillation under

vacuum, and obtained as a vile-smelling yellow oil. This

selenocyanate (244) was heated, as before, with triethylamine in

the presence of 2,3-dimethyl-1,3-butadiene to give the cycloadduct

(249) in 43% yield (Scheme 90). This would suggest that a

mechanism involving the production of the cyclopentadiene

cycloadduct (230) is involved, since cyclopentadiene is generally

much more reactive than 2,3-dimethyl-1,3-butadiene[45]   . Bearing

in mind the thermal stability of (230), as is now known[98]   , it is

difficult to draw any clear conclusions, because repeated attempts

to effect El Naggar's synthesis of (248) produced, at the best only

minimal amounts of the cyclopropane derivative (248). The reason for

this remains unclear.
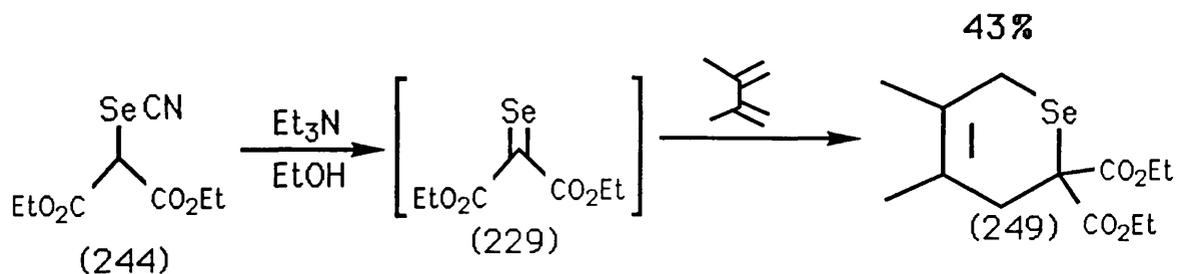
Scheme 90

Fortunately, when the selenocyanate (244) was treated with base

in dichloromethane ^{97} , the selenoketone (229) could be

successfully trapped in situ both with cyclopentadiene and with

2,3-dimethyl-1,3-butadiene at room temperature overnight

(Scheme 91).

Scheme 91
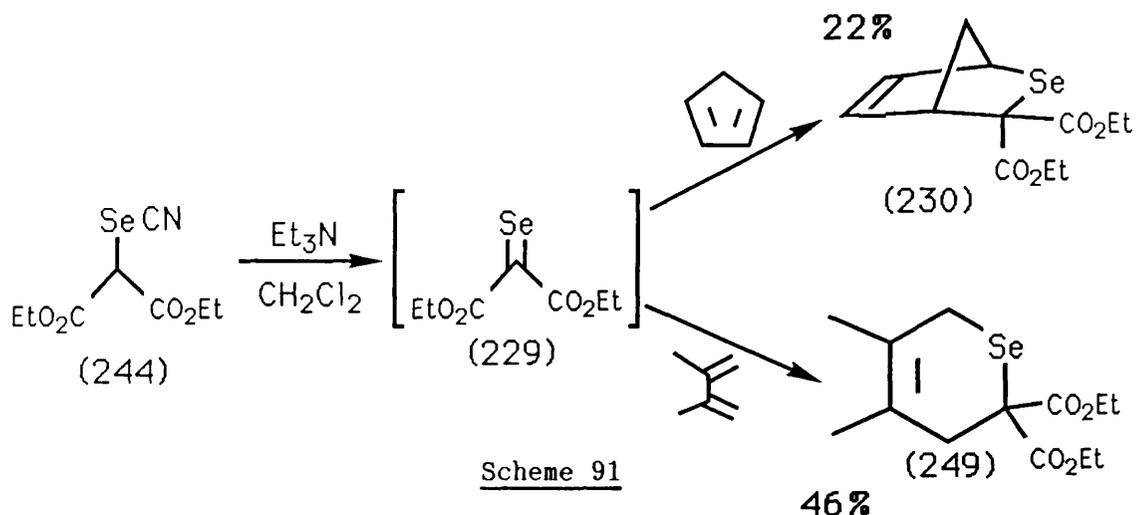
However, yields of (230) were disappointing, and purification by

t.l.c. was difficult, though possible, and reproducibility has

since proven to be a problem. Because of this low stability, a

competition experiment between the two dienes for the selone (229)

could not be done, nor could the cyclopentadiene adduct be used to

attempt to generate (229) by the retro-Diels-Alder reaction, and

transfer the selone to another diene. The only experiments

performed on the small quantities of (230) available allowed its

stability to be tested exhaustively. Neither heating (230) in

refluxing toluene, nor in refluxing ethanol in the presence of

triethylamine (6 mol. equiv.), had any effect and the cycloadduct (230) was recovered quantitatively. This stablilty, similar to the conditions in Scheme 89 suggests that the cyclopropane (248) is not produced by Path B or C. Despite this, the isolation of the 2,3-dimethyl-1,3-butadiene adduct (249) is clear evidence for the production of the selone (229) under these conditions. Unfortunately, this leaves the mechanism of formation of the cyclopropane (248) (Scheme 89) still unresolved.

(c)   APPROACHES FROM THE SELENOSULPHATE (250).

An alternative route to the cyclopentadiene adduct (230) was

sought.   Treatment of diethyl bromomalonate with potassium

selenosulphate in 75% aqueous ethanol gave the selenosulphate (250)

(Scheme 92).   However, (250) proved not to be isolable, and was

generated and used in solution in a "one-pot" reaction.   On

treatment with triethylamine, in 75% aqueous ethanol, the

selenoketone (229) was formed and trapped in situ with

cyclopentadiene (5 mol. equiv.) to give (230), or with

2,3-dimethyl-1,3-butadiene (5. mol. equiv.) to give (249), both in

low yields (<10%) (Scheme 92).
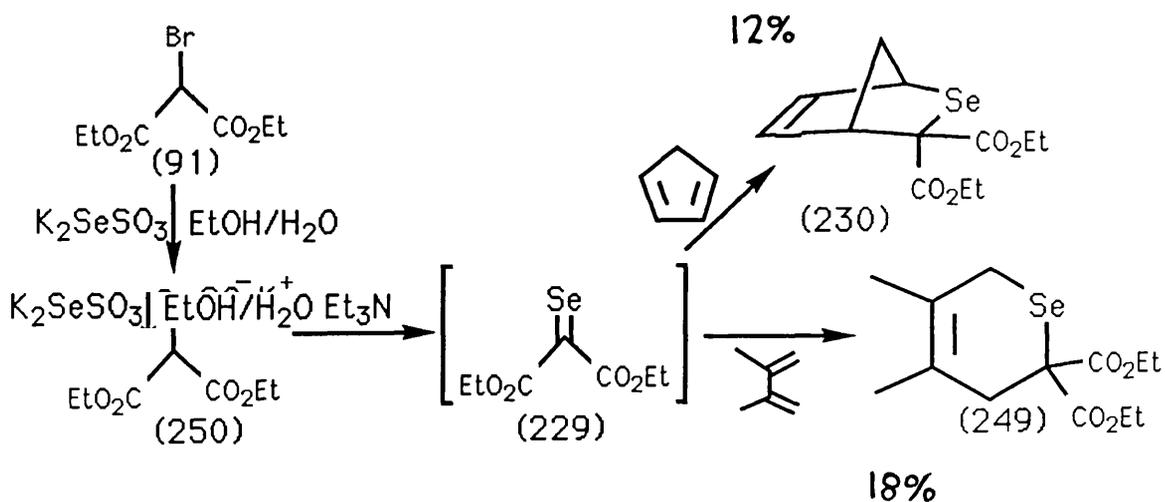
Scheme 92

Once again the reproducibility of these reactions proved to be
disappointingly poor, and insufficient quantities of (230) were
obtained to permit experiments on the projected retro-Diels-Alder
reaction.

On one occasion, a sample of the crude product from the reaction
of the selenosulphate (250) with cyclopentadiene, in the presence
of triethylamine, exibited signals for the presence of the
cycloadduct (230) in the ^{1}H n.m.r. spectrum. Also precipitated
selenium, formed as a byproduct was apparently present, giving the
mixture a black colour. This mixture was stored for approximately
one year, and then purified. However, none of the cycloadduct
(230) was isolated, instead a small amount of the diselenide (252)
was obtained (Scheme 93).
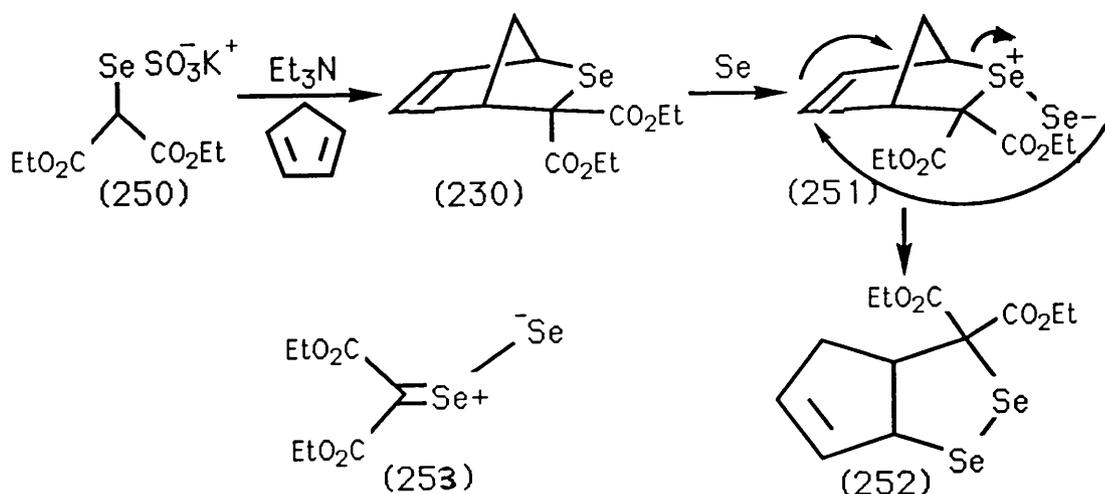
Scheme 93

Figure 2.   Mass Spectrum of (252).
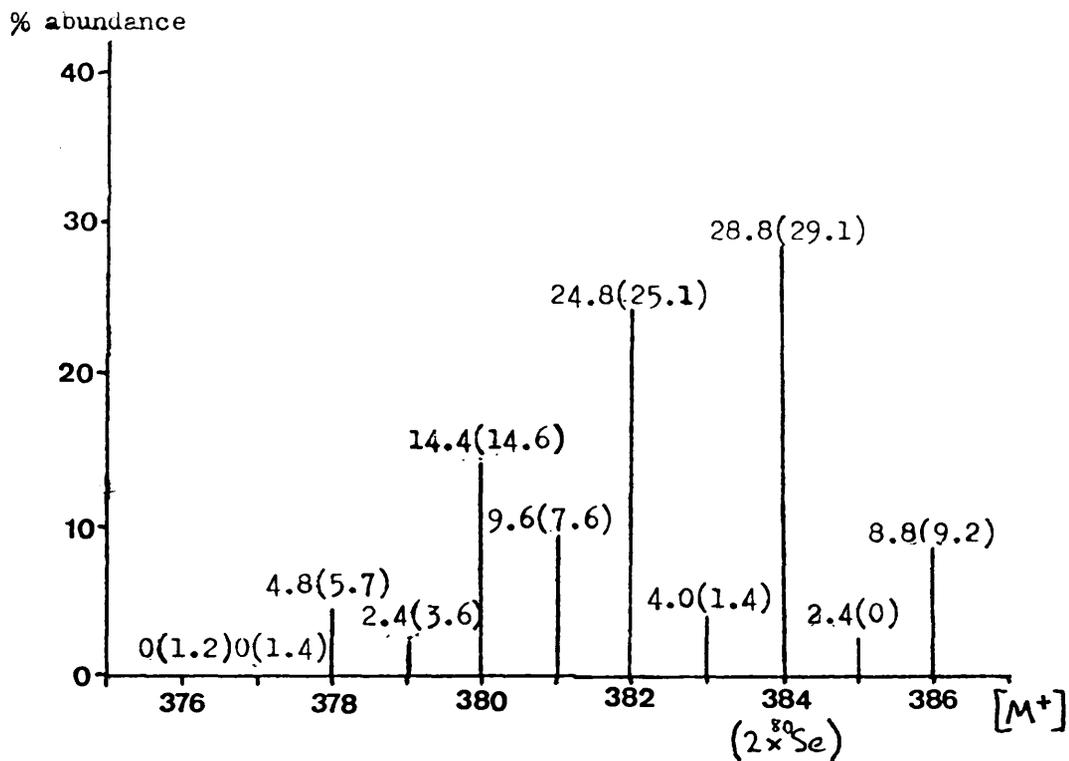
Notes.

Observed M^+ peaks are given as percentage intensities (totalling 100%) with calculated natural abundances (2 x Se) in brackets.

Natural abundance of selenium:-

[74]Se(0.87%), [76]Se(9.0%), [77]Se(7.6%), [78]Se(23.5%), [80]Se(49.8%), [82]Se(9.2%)

The composition of this oily product (252) was determined to be

$C_{12}H_{16}O_4Se_2$, initially by microanalaysis. Mass spectrometry

showed the isotopic distribution pattern unambiguously associated

with 2 selenium atons per molecule[121] (Figure 2), the small

discrepancies being attributable to the small natural abundance of
^{13}C, which becomes significant for a C_{12} molecule. From this

formula, two possible structures were considered (252) and (254).
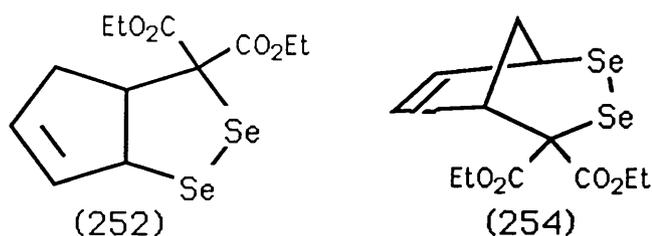
Structure (252) was assigned to the byproduct using ^1H and ^{13}C

n.m.r. spectroscopy, with the aid of data on related compounds

(Table 7). Most significantly, the coupling constant of the

methylene group was measured as 16.9Hz, which is similar to the

value of 17.8Hz observed for the sultene (174), and differs from

the value of 12Hz in the cyclopentadiene adduct (230). This

established the structure (252) for the diselenide. This structure

is formally a cycloadduct of cyclopentadiene and the 1,3-dipole

(253). However it is not known whether (252) was formed as a

byproduct in the original reaction, or by decomposition of the

Table 7. ^{1}H and ^{13}C n.m.r. data for the diselenide (252) and related compounds. [δ (CDCl)]

Compounds (252), (174):

nucleus	(252)	(174)
1-H	5.09	5.54
5-H	obscured	3.63
6-H$_{ex}$	2.52 J 16.9Hz	2.56 J 17.8Hz
6-H$_{en}$	2.33 J 16.9Hz	2.19 J 17.8Hz
C-1	60.4	97.6
C-4	59.7	76.0
C-5	53.4	48.7
C-6	36.7	36.1

Compounds (230), (138):

nucleus	(230)	(138)
1-H	4.42	obscured
4-H	3.61	3.62
7-H$_a$	2.23 J 12Hz	3.04 J 12Hz
7-H$_b$	1.97 J 12Hz	2.35 J 12Hz
C-1		47.8
C-3		83.0
C-4		69.0
C-7		45.7

cyclopentadiene adduct (230) on prolonged storage with selenium.
One proposed mechanism involves the <u>endo</u> compound (251) as an
intermediate (Scheme 93). This is essentially the same as the
reaction of the <u>endo</u>-sulphoxides formed by Block et al [72] , and
also finds analogy with the homologation of allylic sulphides when
heated with elemental sulphur [122] , also involving a sigmatropic
rearrangment (Scheme 94).

(255)   (256)

* = labelled atom
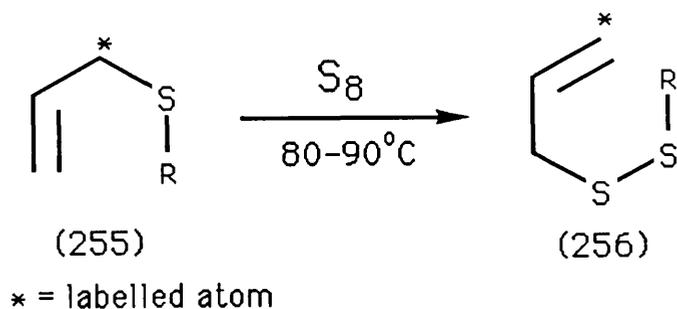
Scheme 94

CONCLUSIONS.

The cycloadducts of diethyl selenoxomalonate (229) proved to be difficult to synthesise, but the cyclopentadiene adduct (230) and the 2,3-dimethyl-1,3-butadiene adduct (249) were made both from the selenocyanate (244) and the selenosulphate (250) in poor to moderate yields. Reproducibility was, however, poor and the results were therefore unsatisfactory. The generally better yields of cycloadduct achieved with 2,3-dimethyl-1,3-butadiene than with cyclopentadiene are rather unusual, as cyclopentadiene is usually the more reactive diene [45]. It may be that cyclopentadiene reacts directly with the selenoketone precursor. Perhaps this might also explain the anomalous formation of the cyclopropane derivative.[119]

CHAPTER 4

EXPERIMENTAL SECTION.

GENERAL PROCEDURES.

Melting points were measured with a Reichert hot-stage apparatus and are uncorrected. [1]H N.m.r. spectra were recorded on a variety of instruments; 90MHz spectra were recorded on a Perkin-Elmer R32 continuous wave spectrometer, 200MHz spectra on Bruker WP200 SY instruments, in the pulsed F.T. mode. [13]C N.m.r. spectra were recorded on a Varian XL-100 spectrometer at 25.1MHz, and ^{13}C DEPT spectra on the Bruker instruments at 50.3MHz. All n.m.r. spectra were run with the sample dissolved in deuteriochloroform, with (on the low field instruments) tetramethylsilane as the internal standard, or (on the high field instruments) residual chloroform as the internal standard. The high field spectra were run by Dr. D. S. Ryecroft, Mr. J. H. Gall, and Mr. J. A. McIver. High resolution mass spectra were recorded on an AEI-GEC 9 mass spectrometer by Mr T. Richie. Infrared spectra were recorded on Perkin Elmer 983 and 580 Infrared Spectrophotometers by Mr. G. M. McCulloch and staff. Ultraviolet spectra were recorded on a Pye Unicam SP8-100 Ultaviolet Spectrophotometer. Microanalyses were exacted by Mrs. K. Wilson using a KLM Elemental Analyser, and titrometric techniques.

Analytical thin layer chromatography (t.l.c.) was carried out on 0.2mm plastic-backed silica gel 60 F$_{254}$ plates, commercially available from Merck. Spots were located by u.v. light and/or

immersion of the eluted plates in iodine vapour. Preparative
t.l.c. separations were carried out on 20 x 20cm glass plates
coated with a 1mm layer of silica gel GF_{254}, available from Fluka.
Organic solutions were dried with anhydrous magnesium sulphate.
Solvents were evaporated on a Buchi Rotavapor evaporator at water
pump pressures. Compounds were dried in a vacuum desiccator over
silica gel (except where phosphorus pentoxide is used to remove
pyridine) at oil-pump pressures.

PREPARATION OF CYCLOADDUCTS OF DIETHYL THIOXOMALONATE (46).

Preparation of Diethyl 3,6-Dihydro-4,5-dimethylthiopyran-

-2,2-dicarboxylate (47) from Diethyl Oxomalonate (48).

Diethyl oxomalonate (2.08g, 11.7mmol) in dry pyridine (25ml) was
added dropwise over 10min to a refluxing solution of phosphorus
pentasulphide (0.99g, 4.45mmol) and 2,3-dimethyl-1,3-butadiene
(5.12g, 62.4mmol) in dry pyridine (100ml) in a nitrogen atmosphere.
Refluxing was maintained for a further 1h, then the solution was
cooled, treated with 5% hydrochloric acid (100ml) and left to stand
for 10min. This mixture was extracted with diethyl ether (100ml)
and the ether layer was then washed successively with 5%
hydrochloric acid (2 x 50ml), 5% aqueous sodium hydrogen carbonate
(50ml), and water (50ml). The ether layer was then dried
(magnesium sulphate) and filtered. The filtrate was evaporated to
dryness under reduced pressure and the residue dried over
phosphorus pentoxide under vacuum to give a yellow oil (2.48g).
This oil was fractionally distilled to yield the cycloadduct (47)[29]
(1.94g, 56%), b.p. 112°C (0.2mm Hg). [Found: C, 57.35; H, 7.76; S,
12.10%; m/z 272.1074. Calc. for $C_{13}H_{20}O_4S$: C, 57.33, H, 7.40; S,
11.73%; M^+, 272.1076.]; ν_{max}(thin film) 1735cm^{-1}; δ_H (90MHz) 1.23(t,
J 7Hz, OCH_2CH_3), 1.70(bs, 4- and 5-Me), 2.67(bs, 3-H), 3.06(bs,
6-H), 4.22(q, J 7Hz, OCH_2CH_3); δ_C(DEPT 50.3MHz) 13.9(2 x OCH$_2$$CH_3$),

19.1 & 20.0(4- and 5-Me), 30.8(C-3), 37.7(C-6), 56.7(C-2),

62.2(2 x O$\underline{C}$H$_2$CH$_3$), 122.4 & 125.4(C-4 and -5), 168.8(2 x CO$_2$).

Preparation of Diethyl 2-Thiabicyclo[2.2.1]hept-5-ene- -3,3-dicarboxylate (93) from Diethyl Oxomalonate (48) [Method A] or Potassium O-Ethyl Xanthate (94) [Method B].

Method A:-

Diethyl oxomalonate (2.01g, 11.6mmol) in dry pyridine (25ml) was

added dropwise over 10min to a refluxing solution of phosphorus

pentasulphide (0.98g, 4.41mmol) and cyclopentadiene (3.71g,

56.2mmol) in dry pyridine (100ml) in a nitrogen atmosphere.

Refluxing was maintained for a further 1h, then the solution was

cooled, treated with 5% hydrochloric acid (100ml) and left to stand

for 10min. This mixture was then worked up as described for (47)

to give a yellow oil (3.63g). This oil was fractionally distilled

to yield the cycloadduct (93) (1.76g, 60%), b.p. 106°C (0.08mm Hg).

[Found: C, 55.95; H, 6.45; S, 12.81%; m/z 256.0770. C$_{12}$H$_{16}$O$_4$S

requires C, 56.23, H, 6.29; S, 12.5%; M$^+$, 256.0770.]; ν_{max}(thin

film) 1750 and 1740cm^{-1}; δ_H (200MHz) 1.23(t, J 7.1Hz, OCH$_2$CH$_3$),

1.24(t, J 6.7Hz, OCH$_2$CH$_3$), 1.81 & 2.05(ABq, J 9.6Hz, 7-H$_2$),

3.85(bs, 1- or 4-H), 4.10(bs, 4- or 1-H), 4.09-4.25(m,2xOCH$_2$CH$_3$),

5.84(dd, J 5.5 and 3.1Hz, 5- or 6-H), 6.52(dd, J 5.5 and 2.9Hz, 6-

or 5-H); δ_c (DEPT 50.3MHz) 13.9 & 14.0(OCH$_2$CH$_3$), 51.4(C-7), 52.5 &

52.8(C-1 and -4), 62.1 & 62.3(OCH$_2$CH$_3$), 131.3 & 140.2(C-5 and -6),

168.8 & 170.2(2 x CO$_2$).

Method B:-

Potassium O-ethyl xanthate (94) (0.65, 4.06mmol) and

cyclopentadiene (2.02g, 30.6mmol) were stirred in acetone (15ml),

cooled in an ice-water bath, and diethyl dibromomalonate (0.52g,

2.05mmol) in acetone (10ml) was added dropwise over 10min to the

solution, which was stirred for a further 2h. The mixture was

allowed to warm to room temperature overnight and was then filtered

and evaporated under reduced pressure. The residue was desiccated

over silica gel under vacuum to give a brown solid (958mg). This

was seperated by preparative t.l.c. with ether-light petroleum

(3:7) as eluant and gave the cycloadduct (93) (310mg, 59%). The

product gave a ^{1}H n.m.r. spectrum identical with the material

produced by method A.

Preparation of Diethyl

9,10-Dihydro-10,9-(epithiomethano)anthracene-12,12-dicarboxylate

(95) from Diethyl Oxomalonate (48).

Diethyl oxomalonate (1.25g, 7.02mmol) in dry pyridine (10ml) was

added dropwise over 10min to a hot solution (70-80°C) of phosphorus

pentasulphide (0.72g, 3.24mmol) and anthracene (6.30g, 35.4mmol) in

dry pyridine (90ml) in a nitrogen atmosphere, with mechanical

stirring. Heating was maintained for a further 1h, then the

solution was cooled, treated with 5% hydrochloric acid (100ml) and

left to stand for 10min. This mixture was extracted with diethyl

ether (150ml) and the ether layer was then filtered to remove

undissolved excess anthracene before being washed successively with

5% hydrochloric acid (2 x 50ml), 5% aqueous sodium hydrogen

carbonate (50ml), and water (50ml). The ether layer was then dried

(magnesium sulphate) and filtered. The filtrate was evaporated to

dryness under reduced pressure and the residue dried overnight over

phosphorus pentoxide under vacuum to give a yellow solid (5.48g).

This was then shaken with methanol (2 x 50ml) and the combined

methanolic extracts were filtered and evaporated under reduced

pressure with heating to give a yellow solid (1.93g). This was

then dissolved in boiling methanol (30ml) and filtered while hot,

then left in a fridge at ca.5°C overnight to crystallise. The

resultant crystals were removed by filtration and washed twice with

light petroleum (2 x 10ml) to give the pure cycloadduct (95)

(617mg, 24%) as white plates, m.p. 150-152°C. [Found: C, 68.35; H,

5.36; S, 8.93%; m/z 368.1075. $C_{21}H_{20}O_4S$ requires: C, 68.46, H,

5.47; S, 8.70%; M^+ 368.1078.]; ν_{max}(thin film) 1745cm^{-1}; δ_H

(200MHz) 1.16(t, J 7.1Hz,2 x OCH$_2$CH$_3$), 4.06(ABq, J 10.8 and 7.2Hz,

OCH_2CH_3), 4.10(ABq, $\underline{J}$ 10.8 and 7.1Hz, OCH_2CH_3), 5.14(s, 9- or

10-H), 5.34(s, 10- or 9-H), 7.1-7.5(m, Ar-H);

δ_C (DEPT 50.3MHz) 13.8(2 x $OCH_2\underline{C}H_3$), 46.7 & 50.7(C-9 and -10),

62.3(2 x $O\underline{C}H_2CH_3$), 68.6(C-12), 122.0-143.1(Ar), 168.2(2 x CO_2).

TRANSFER REACTONS OF DIETHYL THIOXOMALONATE (46).

(a) From the anthracene adduct (95)

i) to give the cyclopentadiene adduct (93).

The anthracene adduct (95) (84.0mg, 0.23mmol) and

cyclopentadiene (84.4mg, 1.28mmol) were refluxed in dry toluene

(20ml), under a nitrogen atmosphere, for 1h. The solution was

cooled and evaporated to dryness under reduced pressure with

heating, and the residue was dried over silica gel under vacuum to

give a yellow solid (132mg), which was purified by preparative

t.l.c. using dichloromethane-light petroleum (1:1) as elutant to

give the cycloadduct (93) (49.3mg, 84%) as a yellow oil. The [1]H

n.m.r. spectum was identical to that of (93) made from (48).

ii) to give the 2,3-dimethyl-1,3-butadiene adduct (47).

The anthracene adduct (95) (150mg, 0.41mmol) and

2,3-dimethyl-1,3- -butadiene (169mg, 2.06mmol) were refluxed in dry

toluene (30ml), under a nitrogen atmosphere. for 1h. The mixture

was worked up as in i) to   give, after preparative t.l.c., the

cycloadduct (47) (33.6mg, 72%) as a yellow oil. The [1]H n.m.r.

spectum was identical to that of (47) made from (48).

(b) From the cyclopentadiene adduct (93) to give the
2,3-dimethyl-1,3-butadiene adduct (47).

The cyclopentadiene adduct (93) (105mg, 0.41mmol) and
2,3-dimethyl-1,3- butadiene (210mg, 2.6mmol) were refluxed in dry
toluene (20ml) for 4h.   The mixture was then cooled and evaporated
to dryness under reduced pressure with heating and desiccated over
silica gel under vacuum to give (47) as a yellow oil (110mg, 99%).
The ^{1}H n.m.r. spectum was identical to that of (47) made from (48).

(c) Competition Experiment.

The anthracene adduct (95) (69.6mg, 0.19mmol), cyclopentadiene
(44.2mg, 0.67mmol) and 2,3-dimethyl-1,3-butadiene (55.4mg,
0.68mmol) were refluxed in dry toluene (20ml), under a nitrogen
atmosphere. for 1h.   The solution was cooled and evaporated to
dryness under reduced pressure with heating, and the residue was
dried over silica gel under vacuum to give a yellow solid.
Integration of the ^{1}H n.m.r. spectrum (90MHz) gave the ratio of
(93) to (47) as 3:2.

Control experiment:- the cyclopentadiene adduct (42.7mg,

0.17mmol) and 2,3-dimethyl-1,3-butadiene (41.1mg, 0.50mmol) were

refluxed in dry toluene (15ml), under a nitrogen atmosphere, for

1h. The solution was cooled and evaporated to dryness under

reduced pressure with heating, and the residue was dried over

silica gel under vacuum to give a yellow solid. Integration of the

[1]H n.m.r. spectrum (90MHz) gave the ratio of (93) to (47) as 2:3.

(d) Measurement of rates of transfer

In General:-

An anthracene adduct (1 mol. equiv.) and

2,3-dimethyl-1,3-butadiene (10 mol. equiv.) were dissolved in dry

toluene in a standard flask (50.0ml). Eight portions (2.0ml each)

were taken and arranged in separate test-tubes, each fitted with a

nitrogen-filled balloon. The test-tubes were suspended in a

constant volume, boiling water bath at 100±1°C and removed at set

time-intervals and cooled immediately in ice-water.

The portions were than each diluted with hexane in individual

standard flasks (10.0ml) and the amount of liberated anthracene

determined by ultaviolet spectroscopy. All absorbances were

measured at λ_{max} 355.0nm in a 10mm cell. The absorbances were taken

from 0min and at regular intervals until 24h (taken as complete
reaction).

i) from the anthracene adduct (27) of ethyl thioxoacetate (28).

The anthracene adduct (27) (12.6mg, 0.044mmol) and
2,3-dimethyl-1,3- butadiene (35.9mg, 0.44mmol) were used as
described above. The reaction was thus shown to be approximately
first-order with respect to the concentration of (27), with a
rate-constant, k, of 1.06 x 10^{-4} s^{-1}.

ii) from the anthracene adduct (95) of diethyl thioxomalonate (46).

The anthracene adduct (95) (23.6mg, 0.064mmol) and
2,3-dimethyl-1,3- butadiene (51.4mg, 0.63mmol) were used as
described previously. The reaction was thus shown to be
approximately first-order with respect to the concentration of
(95), with a rate-constant, k, of 3.28 x 10^{-4} s^{-1}.

(e) Regioselectivity of transfer reactions of diethyl

thioxomalonate (46)

i) to 2-(trimethylsiloxy)buta-1,3-diene to give (98).

The anthracene adduct (95) (144mg, 0.39mmol) and

2-(trimethylsiloxy)buta- 1,3-diene (0.10ml, 1.0mmol) were refluxed

in dry toluene, for 1h, under nitrogen, then the solution was

cooled and evaporated under reduced pressure with heating to give a

yellow solid (290mg), which was determined by n.m.r. to be the

moisture-sensitive adduct (98). δ_H (200MHz) 0.17(s, Me_3SiO),

1.27(t, $\underline{J}$ 7Hz, 2 x OCH_2CH_3), 2.89(dt, $\underline{J}$ 4.5, 2.5Hz, 3-H_2), 3.12(d,

$\underline{J}$ 1.4Hz, 6-H_2), 4.22(q, $\underline{J}$ 7Hz, 2 x OCH_2CH_3), 4.95(t, $\underline{J}$ 4.5Hz, 4-H); δ_C

(DEPT 50.3MHz) 1.85(Me_3SiO), 13.8(2 x OCH_2CH_3), 28.3(C-3),

32.3(C-6), 55.4(C-2), 62.3(2 x OCH_2CH_3), 102.8(C-4), 146.2(C-5),

168.2(2 x CO_2). This crude product was dissolved in THF (10ml) and

potassium fluoride (58mg, 0.85mmol) and three drops of water (ca.

200mg) was added. The solution was stood at room temperature for

24h, and then evaporated to dryness under reduced pressure. The

resultant solid was extracted with dichloromethane (20ml), and the

solution washed with water (2 x 20ml), and dried (magnesium

sulphate), filtered and evaporated to dryness under reduced

pressure. Extraction of the resultant solid with methanol (20ml)

gave, after desiccation, an orange solid (145mg), which was

purified by preparative t.l.c. using dichloromethane/light

petroleum (2:3) as elutant. This gave diethyl

5-oxothiane-2,2-dicarboxylate (99) as a yellow oil (52mg,

51%). [Found m/z 260.0713. $C_{11}H_{16}O_5S$ requires M^+ 260.0711.];

ν_{max} (thin film) 1730cm^{-1}; δ_H (200MHz) 1.24(t, J 7.1Hz, 2 x OCH_2CH_3),

2.60 & 2.71(m, 3- and 4-CH_2), 3.30(s, 6-H_2), 4.24(q, J 7.1Hz, 2

x OCH_2CH_3); δ_C (DEPT 50.3MHz) 13.9(2 x OCH_2CH_3), 33.2 & 35.7 &

36.4(m, 3- and 4- and 6-CH_2), 56.0(C-2), 62.7(2 x OCH_2CH_3),

168.4(2 x CO_2), 203.0(C-5).

ii) to 1-acetoxy-1,3-butadiene to give (97).

The anthracene adduct (95) (95mg, 0.26mmol) and

1-acetoxy-1,3-butadiene (94mg, 0.82mmol) were refluxed in toluene,

for 1 h, under nitrogen, and then cooled and evaporated to dryness

under reduced pressure with heating. The resultant solid was

desiccated under vacuum to give a white solid (116mg), which gave,

after preparative t.l.c. using dichloromethane/light petroleum

(1:1) as elutant, diethyl 3-acetoxy-3,6-dihydrothiapyran-

-2,2-dicarboxyate (97) as an orange oil (48mg, 58%). [Found m/v

302.0817. $C_{13}H_{18}O_6S$ requires M 302.0819.]; ν_{max} (thin film) 1750,

1735cm^{-1}; δ_H (90MHz) 1.23(t, J 7Hz, 2 x OCH_2CH_3), 2.00(s, AcO),

3.16(bs, 6-H_2), 4.24(q, J 7z, 2 x OCH_2CH_3), 5.83 & 6.15(m, 4- and

5-H), <u>ca</u>.6.1(3-H).

(f) 'ene' reaction of diethyl thioxomalonate (46) to give
(-)-6,6-dimethyl-2-(diethyl-3,3-dicarboxylate-2-thiapropane)-
-bicyclo[3.3.1]hept-2-ene (101).

i) from the anthracene adduct (95) of diethyl thioxomalonate (46).

The anthracene adduct (95) (260mg, 0.71mmol) and (-)-β-pinene
(250mg, 1.8mmol) were refluxed in dry toluene (25ml), for 1h, under
nitrogen. The solution was cooled and evaporated to dryness under
reduced pressure with heating, then desiccated under vacuum to give
a yellow solid (450mg). Preparative t.l.c. using
dichloromethane/light petroleum (1:1) as elutant gave (101) as a
yellow oil (140mg, 61%). [Found: C, 62.34; H, 7.92; S, 10.01%; <u>m</u>/<u>z</u>
326.1571. $C_{17}H_{26}O_4S$ requires C,62.55; H, 8.03; S, 9.88%; M^+
326.1565.]; $[\alpha]_D^{22}$ -8°(MeOH); ν_{max} (thin film) 1745, 1730cm^{-1};
δ_H (90MHz) 0.80 & 1.24(s, 2 x 6-Me), 1.26(t, <u>J</u> 7Hz, 2 x OCH$_2$CH$_3$),
2.01-2.45(m, 1- and 5- H, 4- and 7-H$_2$), 3.25(bs, CH$_2$S), 4.11(s,
CHS), 4.22(q, <u>J</u> 7Hz, 2 x OCH$_2$CH$_3$), 5.47(bs, 3-H).

ii) from the cyclopentadiene adduct (93) of diethyl thioxomalonate

(46).

The cyclopentadiene adduct (93) (114mg, 0.45mmol) and (-)-β

-pinene (180mg, 1.3mmol) were refluxed in dry toluene (10ml), for

4h, under nitrogen. The solution was cooled and evaporated to

dryness under reduced pressure with heating, then desiccated under

vacuum to give a brown oil (189mg). Preparative t.l.c. using

dichloromethane/light petroleum (1:1) as elutant gave (101) as a

yellow oil (43mg, 30%). The ^{1}H n.m.r. spectrum was identical to

that of material produced in i).

PREPARATION OF CYCLOADDUCTS OF DIETHYL THIOXOMALONATE $\underline{S}$-OXIDE.

Preparation of Diethyl 3,6-Dihydro-4,5-dimethylthiopyran-2,2-
-dicarboxylate $\underline{S}$-oxide (149).

$\underline{m}$-Chloroperoxybenzoic acid (mCPBA) (1.15g, 6.69mmol) in
dichloromethane (10ml) was added dropwise with shaking, over 15min,
to a solution of (47) (1.47g, 5.40mmol) in dichloromethane (10ml)
at room temperature. The solution was left standing for 1h, then
diluted with dichloromethane (30ml), and washed with 10% aqueous
potassium sulphite (2 x 30ml), then water (30ml). The
dichloromethane solution was then dried (magnesium sulphate),
filtered and evaporated to dryness under reduced pressure, and
desiccated over silica gel under vacuum to give the $\underline{S}$-oxide (149)
as a yellow oil (1.41g, 91%)[55,73,74], b.pt. 140°C (0.1mm Hg). [Found:
C, 54.11; H, 6.81; S, 11.41%; $\underline{m/z}$ 288.1032. Calc. for $C_{13}H_{20}O_5S$
C, 54.15; H, 6.99; S, 11.12%; M^+ 288.1032.]; ν_{max} (thin film)
1750, 1730cm-¹ ; δ_H (90MHz) 1.15 & 1.25(2 x t, $\underline{J}$ 7Hz, 2 x $OC\underline{H_2}C\underline{H_3}$),
1.63 & 1.96(s, 5- and 6-Me), 2.78-3.52(m, 3-H_2 and 6-H_2), 4.15 &
4.25(2 x q, $\underline{J}$ 7Hz, 2 x $OC\underline{H_2}$ CH_3); δ_C (DEPT 50.3MHz) 13.5(2 x
$OC\underline{H_2}\underline{C}\underline{H_3}$), 18.8 & 19.9(4- and 5- Me), 27.7(C-3), 50.6(C-6), 62.2 &
62.5(2 x $O\underline{C}H_2CH_3$), 70.0(C-2), 115.7 & 124.9(C-4 and -5), 184.9 &
185.3(2 X CO_2).

Preparation of <u>exo</u>-Diethyl 2-Thiabicyclo[2.2.1]hept-5-ene-
-3,3-dicarboxylate <u>S</u>-Oxide (173).

<u>m</u>-Chloroperoxybenzoic acid (mCPBA) (0.94g, 5.47mmol) in
dichloromethane (10ml) was added dropwise with shaking, over 15min,
to a solution of (93) (1.29g, 5.04mmol) in dichloromethane (10ml)
at room temperature. The solution was left standing for 1h, then
diluted with dichloromethane (30ml), and washed with 10% aqueous
potassium sulphite (2 x 30ml), then water (30ml). The
dichloromethane solution was then dried (magnesium sulphate),
filtered and evaporated to dryness under reduced pressure, and
desiccated over silica gel under vacuum to give the <u>S-oxide (173)</u>
as a yellow oil (1.21g, 89%), b.pt. >200°C (0.1mm Hg). [Found:
C, 52.74; H, 6.20; S, 11.80%; <u>m/z</u> 277.0715. $C_{12}H_{16}O_5S$ requires
C, 52.93; H, 5.92; S, 11.77%; M$^+$ 272.0719.]; ν_{max} (thin film)
1735cm-' ; δ_H (90MHz) 1.14 & 1.24(2 x t, <u>J</u> 7Hz, 2 x OCH$_2$CH$_3$),
2.35(dt, <u>J</u> 12, 2Hz, 7-H), 3.04(d, <u>J</u> 12Hz, 7-H), 3.62(bs, 1- or
4-H), 4.02-4.32(m, 1- or 4-H and 2 x OCH$_2$CH$_3$), 5.94 & 6.29(m, 5-
and 6-H); δ_C (DEPT 50.3MHz) 13.9 & 14.0(2 x OCH$_2$CH$_3$), 45.7(C-7),
47.8(C-4), 62.3 & 62.7(2 x OCH$_2$CH$_3$), 69.0(C-1), 83.0(C-3), 130.2 &
141.1(C-5 and -6), 164 & 166(2 X CO$_2$).

Preparation of Diethyl 9,10-Dihydro-10,9-(epithiomethano)anthracene-
-12,12-dicarboxylate S-Oxide (172)

(a) with mCPBA in dichloromethane.

m-Chloroperoxybenzoic acid (mCPBA) (238mg, 1.38mmol) in

dichloromethane (5ml) was added dropwise with shaking, over 15min,

to a solution of (95) (410mg, 1.12mmol) in dichloromethane (10ml)

at room temperature. The solution was left standing for 1h, then

diluted with dichloromethane (30ml), and washed with 10% aqueous

potassium sulphite (2 x 30ml), then water (30ml). The

dichloromethane solution was dried (magnesium sulphate),

filtered and evaporated to dryness under reduced pressure, and

desiccated over silica gel under vacuum to give the S-oxide (172),

recrystallised from methanol as white plates (336mg, 79%), m.pt.

94-98°C. ν_{max} (thin film) 1735cm-1 ; δ_H (200MHz) 1.10 & 1.20(2 x

t, J 7Hz, OCH$_2$CH$_3$), 3.91-4.36(m, 2 x OCH$_2$CH$_3$), 5.26 & 5.78(2 x s,

9- and 10-H), 7.21-7.56(m, Ar-H); δ_C (DEPT 50.3MHz) 13.9(2 x

OCH$_2$CH$_3$), 49.7(C-9), 62.5(2 x OCH$_2$CH$_3$), 68.1(C-10), 82.7(C-12),

125.3-132.9(Ar), 162.9 & 165.8(2 x CO$_2$).

(b) with peracetic acid in dichloromethane.

A solution of peracetic acid (34% w/w in acetic acid) (1.03g,
4.61mmol) in dichloromethane (5ml) was added dropwise with shaking,
over 10min, to a solution of (95) (1.41g, 3.67mmol) in
dichloromethane (15ml) at room temperature. The solution was left
standing for 1h, then diluted with dichloromethane (30ml), washed
with 5% aqueous sodium hydrogen carbonate (2 x 50ml), and water
(50ml). The dichloromethane solution was then dried (magnesium
sulphate), filtered and evaporated to dryness under reduced
pressure, and desiccated over silica gel under vacuum to give the
S-oxide (172) as white plates (ex. MeOH) (1.29g, 88%). The material
had an identical ^{1}H n.m.r. spectrum to material made in (a).

(c) with peracetic acid in diethyl ether.

A solution of peracetic acid (27% w/w in acetic acid) (201mg,
0.75mmol) in diethyl ether (5ml) was added dropwise with shaking,
over 10min, to a solution of (95) (270mg, 0.73mmol) in diethyl
ether (30ml) at room temperature. The solution was left standing
for 1h, then evaporated to dryness, redissolved in dichloromethane
(50ml) and worked up as in (b) to give (172) as white plates
(242mg, 86%). The material had an identical ^{1}H n.m.r. spectrum to
material made in (a).

Preparation of Diethyl 5-Oxothiane-2,2-dicarboxylate S-Oxide (183).

A solution of peracetic acid (27% w/w in acetic acid) (80mg,
0.30mmol) in diethyl ether (5ml) was added dropwise with shaking,
over 10min, to a solution of (98) (66mg, 0.25mmol) in diethyl
ether (30ml) at room temperature. The solution was left standing
for 1h, then evaporated to dryness, redissolved in dichloromethane
(50ml) and worked up as in (b) to give the S-oxide (183) as a pale
yellow oil (54mg, 77%). δ_H (200MHz) 1.29(t, J 7.1Hz, OCH_2CH_3),
1.31(t, J 7.1Hz, OCH_2CH_3), 2.50-3.22(m, 3-H and 4-H_2), 3.64(dd,
J 14.5, 1.3Hz, 6-H_2), 4.09(d, J 14.4Hz, 6-H_2), 4.25-4.41(m, 2 x
OCH_2CH_3); δ_C (DEPT 50.3MHz) 13.9Hz(2 x OCH_2CH_3), 25.6(C-3),
37.1(C-4), 57.6(C-6), 63.4 & 63.6(2 x OCH_2CH_3), 71.3(C-2), 164.2 &
165.9(2 x CO_2).

TRANSFER REACTONS OF DIETHYL THIOXOMALONATE $\underline{S}$-OXIDE.

(a) From the anthracene adduct (172)

i) to cyclopentadiene in refluxing toluene to give the sultene (174).

The anthracene adduct (172) (60mg, 0.16mmol) and cyclopentadiene (53mg, 0.81mmol) were refluxed in dry toluene (10ml), under a nitrogen atmosphere, for 1h. The solution was cooled and evaporated to dryness under reduced pressure with heating. The residue was extracted with cold methanol (2ml) and the methanolic solution was filtered and evaporated to dryness under reduced pressure, then desiccated over silica gel under vacuum to give the sultene (174) as a yellow oil (30mg, 71%), b.pt. >250°C (0.1mm Hg) [Found: $\underline{m}/\underline{z}$ 272.0724. $C_{12}H_{16}O_5S$ requires M^+ 272.0718.]; ν_{max} (thin film) 1790, 1735cm^{-1} ; δ_H (200MHz) 1.24(t, $\underline{J}$ 7.0Hz, OCH_2CH_3), 1.25(t, $\underline{J}$ 7.2Hz, OCH_2CH_3), 2.19(ddq, $\underline{J}_{en,ex}$ 17.8, $\underline{J}$ 4.6, 2.3Hz, 6_{ex}-H), 2.56(ddt, $\underline{J}_{en,ex}$ 17.8, $\underline{J}$ 8.6Hz, $\underline{J}_{5,6en}=\underline{J}_{8,6en}$ 2.2Hz, 6_{en}-H), 3.63(ddd, $\underline{J}_{1,5}$ 8.5Hz, $\underline{J}_{6ex,5}$ 4.6Hz, $\underline{J}_{6en,5}$ 2.2Hz, 5-H), 4.21(q, $\underline{J}$ 7.1Hz, OCH_2CH_3), 4.23(q, $\underline{J}$ 7.1 Hz, OCH_2CH_3), 5.54(dt, $\underline{J}_{5,1}$ 8.5Hz, $\underline{J}_{8,1}=\underline{J}_{6en,1}$ 2.4Hz, 1-H), 5.68(dt, $\underline{J}_{8,7}$ 5.9Hz, $\underline{J}_{1,8}=\underline{J}_{6en,8}$ 2.2Hz, 8-H), 6.10(dd, $\underline{J}$ 5.9Hz, $\underline{J}_{7,6en}$ 1.9Hz, 7-H); δ_C (25.1MHz) 14.0(2 x OCH_2CH_3), 36.1(C-6), 48.7(C-5), 62.5(2 x OCH_2CH_3), 76.0(C-4), 97.6(C-1),

128.2(C-8), 138.2(C-7), 166.0 & 168.8(2 x CO_2).

ii) to cyclopentadiene in refluxing benzene to give 2:1 (173) and (174).

The anthracene adduct (172) (31mg, 0.08mmol) and cyclopentadiene (27mg, 0.42mmol) were refluxed in dry benzene (5ml), under a nitrogen atmosphere, for 40min (reaction complete). The solution was cooled and evaporated to dryness under reduced pressure, with heating, to give a white solid (33mg). This was shown by ^{1}H n.m.r. spectroscopy to contain no starting material (172), but contained anthracene, and a mixture of the exo-cyclopentadiene adduct (173) and the sultene (174) in a ratio of 2:1.

iii) to 2,3-dimethyl-1,3-butadiene to give (149).

The anthracene adduct (172) (68mg, 0.18mmol) and 2,3-dimethyl--1,3-butadiene (73mg, 0.89mmol) were refluxed in dry benzene (15ml), under a nitrogen atmosphere, for 1h. The solution was cooled and evaporated to dryness under reduced pressure, with heating, then desiccated uver silica gel under vacuum to give a yellow solid (88mg). This solid was purified by preparative t.l.c. on a silica plate using diethyl ether as elutant to give the cycloadduct (149) as a yellow oil (32mg, 64%).

(b) From the exo-cyclopentadiene adduct (173) to give the
2,3-dimethyl-1,3-butadiene adduct (149).

The exo-cyclopentadiene adduct (173) (120mg, 0.44mmol) and
2,3-dimethyl-1,3-butadiene (183mg, 2.24mmol) were refluxed in dry
toluene (20ml), under a nitrogen atmosphere, for 1h. The solution
was cooled and evaporated to dryness under reduced pressure, with
heating, then desiccated over silica gel under vacuum to give an
orange oil (127mg). ^{1}H n.m.r. spectroscopy showed ca. 5% of this
mixture to be the sultene (174). This solid was purified by
preparative t.l.c. on a silica plate using diethyl ether as elutant
to give the cycloadduct (149) as a yellow oil (102mg, 80%).

(c) On heating the exo-cyclopentadiene adduct (173) alone.

The exo-cyclopentadiene adduct (173) (3.10g, 11.4mmol) was
refluxed in dry toluene (100ml), under a nitrogen atmosphere, for
1h. The solution was cooled and evaporated to dryness under
reduced pressure, with heating, then desiccated over silica gel
under vacuum to give the sultene (174) as a yellow oil (2.72g,
88%). The ^{1}H n.m.r. spectrum of this material was identical to
that poduced in (a) i).

(d) Competition experiment.

The anthracene adduct (172) (116mg, 0.30mmol), cyclopentadiene

(61mg, 0.92mmol) and 2,3-dimethyl-1,3-butadiene (76mg, 0.93mmol)

were refluxed in dry benzene (20ml), under a nitrogen atmosphere,

for 1h. The solution was cooled and evaporated to dryness under

reduced pressure, with heating, to give a white solid (141mg).

This was shown by ^{1}H n.m.r. spectroscopy to contain no starting

material (172), but contained anthracene, and a mixture of the

exo-cyclopentadiene adduct (173) and the sultene (174) in a ratio

of 2:1. No 2,3-dimethyl-1,3-butadiene adduct (149) was observed.

(e) Measurement of rates of transfer

The anthracene adduct (172) (15.7mg, 0.041mmol) and

2,3-dimethyl-1,3-butadiene (32.9mg, 0.401mmol) were dissolved in

dry benzene in a standard flask (50.0ml). Eight portions (2.0ml

each) were taken and arranged in separate test-tubes, each fitted

with a nitrogen-filled balloon. The test-tubes were suspended in a

thermostatted water bath at 60 C and removed at set time-intervals

and cooled immediately in ice-water.

The portions were than each diluted with hexane in individual

standard flasks (10.0ml) and the amount of liberated anthracene

determined by ultaviolet spectroscopy. All absorbances were

measured at λ_{max} 355.0nm in a 10mm cell. The absorbances was taken

from 0min and at regular intervals until 24h (taken as complete

reaction).

The reaction was thus shown to be approximately first-order with

respect to the concentration of (172), with a rate-constant, k, of

2.82×10^{-4} s^{-1}.

(f) Flash Vacuum Pyrolysis (F.V.P.) of the anthracene adduct (172).

In general:-

The anthracene adduct (172) was dispersed onto freshly dried

Figure 3.   Flash Vacuum Pyrolysis Apparatus.
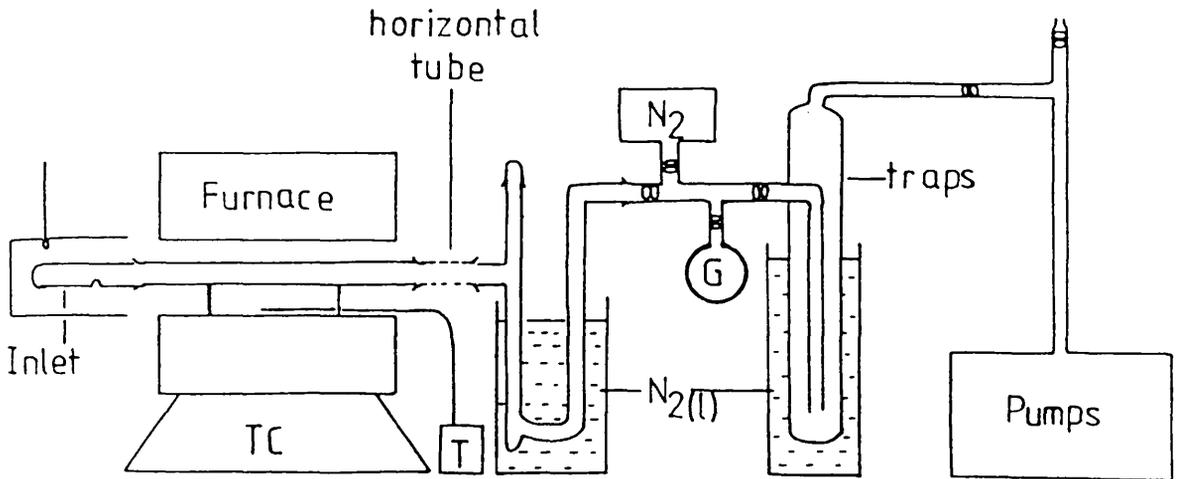
G:Gauges   T:Thermocouple

TC:Temperature control unit

and ground magnesium sulphate by first dissolving (172) in

dichloromethane, then adding the magnesium sulphate, and

evaporating to dryness under reduced pressure and desiccating the

residue over phosphorus pentoxide under vacuum. This sample

was placed in the sample chamber of the F.V.P. apparatus[123]

(Figure 3), the apparatus flushed with nitrogen, and the adduct

(172) was then volatilised under high vacuum by heating the sample

chamber at ca.160°C for 10min. Volatilised (172) then passed

through the oven (preheated to 500°C), and the pyrolysis

product(s) were caught in a cold trap at liquid nitrogen

temperatures (anthracene invariably solidified onto the glass tube

before the cold trap effectively separating it from any other

products). In some experiments, a large excess of either

cyclopentadiene or water was already present in the cold trap,

having previously been distilled into the system under high vacuum.

In all cases byproduct(s) consistent with oligomer(s)/polymer(s) of

the sulphine (148) were obtained. Elemental sulphur was also

always produced (detected on analytical t.l.c. by spraying with 5%

silver nitrate in aqueous acetone).

i) Trapping the sulphine (148) in cold trap in presence of

   cyclopentadiene.

The anthracene adduct (172) (122g, 0.32mmol) on magnesium

sulphate (0.63g) was volatilised and passed through an oven at

500 C (3 x 10-4 mbar), and the more volatile products (free of

anthracene) were trapped in a cold trap in the presence of

cyclopentadiene (212mg, 3.2mmol). The system was filled with

nitrogen to atmospheric pressure and cyclopentadiene (208mg,

3.2mmol) in dichloromethane (10ml) was added to the cold trap under

nitrogen, and the mixture allowed to warm up to room temperature.

The resultant solution was evaporated to dryness under reduced

pressure, and desiccated under vacuum to give a yellow oil (57mg).

^{1}H n.m.r. spectroscopy showed that, from integration of the signals

due to carboxyethyl groups, ca.70% of the sulphine trapped had

formed a cycloadduct with cyclopentadiene (giving the exo-isomer

only). The other ca.30% had formed byproduct(s) related to

oligomer(s)/polymer(s) of the sulphine (analysed by mass

spectroscopy). Only a trace of diethyl malonate was observed in

the ^{1}H n.m.r. spectrum. Preparative t.l.c. of the mixture gave the

exo-cyclopentadiene adduct (173) as a yellow oil (41mg, 47%).

ii) Trapping the sulphine (148) in cold trap in presence of

        water.

The anthracene adduct (172) (92g, 0.24mmol) on magnesium

sulphate (0.94g) was volatilised and passed through an oven at

500°C (2 x 10-4 mbar), and the more volatile products (free of

anthracene) were trapped in a cold trap in the presence of

water (82mg, 4.6mmol). The system was filled with

nitrogen to atmospheric pressure and dichloromethane (10ml) was

added to the cold trap under nitrogen, and the mixture allowed to

warm up to room temperature. The resultant solution was evaporated

to dryness under reduced pressure, and desiccated under vacuum to

give a yellow oil (30mg). ^{13}C & ^{1}H n.m.r. spectroscopy showed that,

from integration of the signals due to carboxyethyl groups, ca.60%

of the sulphine trapped had been hydrolysed to give diethyl

malonate (175). The other ca.40% had formed byproduct(s) related to

oligomer(s)/polymer(s) of the sulphine (as in i)).

iii) Trapping the sulphine (148) in cold trap alone.

The anthracene adduct (172) (89g, 0.23mmol) on magnesium

sulphate (0.92g) was volatilised and passed through an oven at

500°C (2 x 10-4 mbar), and the more volatile products (free of

anthracene) were trapped in a cold trap. The system was filled with

nitrogen to atmospheric pressure and dichloromethane (10ml) was

added to the cold trap under nitrogen, and the mixture allowed to

warm up to room temperature. The resultant solution was evaporated

to dryness under reduced pressure, and desiccated under vacuum to

give a yellow oil (20mg). ^{13}C & ^{1}H n.m.r. spectroscopy showed that,

from integration of the signals due to carboxyethyl groups, ca.40%

of the sulphine trapped had been hydrolysed to give diethyl

malonate (175).   The other ca.60% had formed byproduct(s) related

to oligomer(s)/polymer(s) of the sulphine (as in i)).

(g) Regioselectivity of transfer reactions of diethyl

    thioxomalonate S-oxide (148).

i) in refluxing benzene to give a 4:1 mixture of (183) and (182).

The anthracene adduct (172) (149mg, 0.39mmol) and

2-(trimethylsilyloxy)-1,3-butadiene (0.10ml, 1.0mmol) were refluxed

in dry benzene (35ml) for 1h, under a nitrogen atmosphere.   The

solution was then cooled and evaporated to dryness under reduced

pressure with heating to give a white solid (322mg).   This residue

was dissolved in tetrahydrofuran (10ml) with potassium fluoride

(68mg) and three drops of water (ca. 200mg) and left to stand at

room temperature overnight.   The mixture was evaporated to dryness

under reduced pressure and dissolved in dichloromethane (20ml),

washed with water (2 x 20ml) and dried (magnesium sulphate).   The

solution was filtered, evaporated to dryness and desiccated over

silica gel under vacuum to give an orange solid (138mg) which was

purified by preparative t.l.c. using ethyl acetate-light petroleum

(3:2) as elutant to give an orange oil (51mg, 48%).   This oil was

determined by ^{1}H and ^{13}C n.m.r. to be a 4:1 mixture of the 5-oxo-

isomer (183) and the 4-oxo-isomer (182). The n.m.r. contained

identical peaks to those for (183) made by peracid oxidation of

(98).

ii) in refluxing toluene to give (182).

The anthracene adduct (172) (313mg, 0.82mmol) and

2-(trimethylsilyloxy)-1,3-butadiene (0.25ml, 2.5mmol) were refluxed

in dry benzene (50ml) for 1h, under a nitrogen atmosphere. The

solution was then cooled and evaporated to dryness under reduced

pressure with heating to give a white solid (614mg). This residue

was dissolved in tetrahydrofuran (15ml) with potassium fluoride

(140mg) and four drops of water (ca. 300mg) and left to stand at

room temperature overnight. The mixture was evaporated to dryness

under reduced pressure and dissolved in dichloromethane (40ml),

washed with water (2 x 40ml) and dried (magnesium sulphate). The

solution was filtered, evaporated to dryness and desiccated over

silica gel under vacuum to give a brown solid (326mg) which was

purified by preparative t.l.c. using ethyl acetate-light petroleum

(3:2) as elutant to give an orange oil (66mg, 30%). This oil

was determined by ^{1}H and ^{13}C n.m.r. to be a almost entirely diethyl

4-oxothiane-2,2-dicarboxylate S-oxide (182) (with only a trace of

the 5-oxo-isomer (183)). δ_H (200MHz) 1.2-1.4(m, 2 x OCH$_2$CH$_3$),

2.38-3.20(m, 5-H$_2$ and 6-H$_2$), 3.13(d, J 15.8Hz, 3-H), 3.63(d,

J 15.7Hz, 3-H), 4.1-4.4(m 2 x OC$\underline{H}_2$CH_3); δ_c(DEPT 50.3MHz) 13.9(2 x

OCH$_2$C$\underline{H}_3$), 30.2(C-3), 38.2(C-5), 44.2(C-6), 62.3 & 62.9(2 x

OC$\underline{H}_2$CH$_3$), 70.2(C-2), 163 & 165(2 x CO$_2$).

PREPARATION OF CYCLOADDUCTS OF DIETHYL SELENOXOMALONATE (229).

Preparation of Diethyl Selenocyanatomalonate (244) from Diethyl Bromomalonate (91).

Diethyl bromomalonate (91) (28.71g, 0.120 mol) in ethanol (50ml) was added dropwise over 10min to potassium selenocyanate (32.14g, 0.223mol) in ethanol (200ml) at reflux. This solution was refluxed for a further 1h, and then was cooled and evaporated under reduced pressure with heating to give an orange oil, which was then dissolved with ether (100ml). This solution was washed with 5% aq. hydrochloric acid (2 x 30ml), then with water (2 x 30ml). The ether layer was dried (magnesium sulphate), filtered and evaporated under reduced pressure to give a yellow oil, which was fractionally distilled to give diethyl selenocyanatomalonate (244) (9.39g, 30%) as a yellow oil, b.pt. 85°C (0.1mm Hg). [Found: C, 36.34; H, 3.92%; $\underline{m/z}$(^{80}Se) 264.9856. $C_8H_{11}NO_4Se$ requires C, 36.4; H, 4.2%; M$^+$ (^{80}Se) 264.9855.]; ν_{max}(thin film) 1730cm^{-1} ; δ_H(90MHz) 1.32(t, $\underline{J}$ 7.3Hz, OCH$_2$CH$_3$), 4.33(q, $\underline{J}$ 7.3Hz, OCH$_2$CH$_3$), 4.93(s, HCSe). The first fraction from the distillation contained mainly diethyl malonate, the major byproduct, identified by ^{1}H n.m.r. and boiling point.

Preparation of Diethyl 3,6-Dihydro-4,5-dimethyl-selenopyran-

-2,2-dicarboxylate (249).

(i) from Diethyl Selenocyanatomalonate (2244.

Method A:-

Diethyl selenocyanatomalonate (244) (1.86g, 7.05mmol),

2,3-dimethyl- 1,3-butadiene (1.71g, 20.9mmol) and calcium chloride

dihydrate (0.99g, 6.73mmol) in ethanol (15ml) were heated to

reflux. Triethylamine (0.74g, 7.33mmol) in ethanol (15ml) was

added dropwise over 15min to the refluxing solution. After a

further 1h at reflux, the solution was cooled and evaporated to

dryness under reduced pressure with heating. The residue was

dissolved in chloroform (50ml) and washed with 5% aq. hydrochloric

acid (2 x 50ml), then with water (2 x 50ml). The choroform

solution was dried (magnesium sulphate), filtered and evaporated to

dryness to give a yellow oil (1.87g). Chromatography on a silica

(t.l.c. grade) column with chloroform as elutant gave the

selenopyran (249) (0.97g, 43%) as a yellow oil, b.pt. 115°C (0.03mm

Hg). [Found: C, 48.86; H, 6.21%; $\underline{m}/\underline{z}$(^{80}Se) 320.0527. $C_{13}H_{20}O_4Se$

requires C, 48.9; H, 6.3%; M^+ (^{80}Se) 320.0527.];

ν_{max} (thin film) 1730cm-1 ; δ_H (90Mhz) 1.23(t, $\underline{J}$ 7.3Hz, $OCH_2C\underline{H}_3$),

1.77(bs, 4- and 5-Me), 2.73(bs, 3-H_2), 3.14(bs,6-H_2), 4.20(q, $\underline{J}$

7.3Hz, $OC\underline{H}_2CH_3$).

Method B:-

Diethyl selenocyanatomalonate (244) (170mg, 0.64mmol), and

2,3-dimethyl-1,3-butadiene (213mg, 2.6mmol) were dissolved in

dichloromethane (5ml) at room temperature. Triethylamine (67mg,

0.65mmol) in dichloromethane (5ml) was added dropwise over 15min

with stirring. After a further 24h stirring, the solution was

washed with water (2 x 20ml). The solution was dried (magnesium

sulphate), filtered and evaporated to dryness to give a yellow oil

(102mg). Preparative t.l.c. on a silica plate using ether/light

petroleum (3:7) as elutant gave the selenopyran (249) (96mg, 46%)

as a yellow oil. The ^{1}H n.m.r. spectrum of this oil was identical

with that of material made by method A.

(ii) via Potassium Se,Se-Di(ethoxycarbonyl) Selenosulphate (250).

Potassium sulphite (5.01g, 31.7mmol) and grey selenium (2.07g,

26.2mmol) were heated under reflux in water (50ml) for 30min,

cooled and filtered to give a solution containing potassium

selenosulphate. Diethyl 2-bromomalonate (91) (5.98g, 25.0mmol) in

ethanol (75ml) was added to this solution at room temperature and

the mixture was shaken briefly before addition of

2,3-dimethyl-1,3-butadiene (10.24g, 125mmol) and calcium chloride

dihydrate (3.71g, 25.2mmol) in ethanol (50ml). Lastly,

triethylamine (2.56g, 25.3mmol) in ethanol (25ml) was added

dropwise over 5min with stirring. After a further 1h stirring at
room temperature, the resulting red solution was evaporated to
dryness under reduced pressure with heating. The residue was
dissolved in diethyl ether (50ml) and washed with aq. hydrochloric
acid (50ml) and then water (50ml). The ether layer was dried
(magnesium sulphate), filtered and evaporated to dryness under
reduced pressure to give, after desiccation under vacuum, a yellow
oil (1.82g). Preparative t.l.c. on silica plates using ether/light
petroleum (3:7) as elutant gave the pure selenopyran (249) as a
yellow oil (18%). The ^{1}H n.m.r. spectrum of this oil was identical
with that of material made in (i).

Preparation of Diethyl 2-Selenabicyclo[2.2.1]hept-5-ene-3,3-
-dicarboxylate (230).

(i) from Diethyl Selenocyanatomalonate (244) [Method B].

   Diethyl selenocyanatomalonate (244) (69.2g, 0.26mmol), and
cyclopentadiene (93.8g, 1.42mmol) were dissolved in dichloromethane
(5ml) at room temperature. Triethylamine (34.5mg, 0.34mmol) in
dichloromethane (5ml) was added dropwise over 15min with stirring.
After a further 24h stirring, the solution was washed with water (2
x 20ml). The solution was dried (magnesium sulphate), filtered and

evaporated to dryness to give a yellow oil (97mg). Preparative
t.l.c. on a silica plate using ether/light petroleum (3:7) as
elutant gave the adduct [98] (230) (17.6mg, 22%) as a yellow oil, b.pt.
110°C (0.02mm Hg). [Found: C, 47.58; H, %.39%; m/z (^{80}Se)
304.0207. Calc. for $C_{12}H_{16}O_4Se$: C, 47.54, H, 5.32%; M^+ (^{80}Se)
304.0209.]; ν_{max} (thin film) 1730 and 1755cm-ι; δ_H (90MHz) 1.24 &
1.25(2 x t, J 7Hz, 2 x OCH_2CH_3), 1.97 & 2.23(ABq, J 12Hz, 7-H_2),
3.61(bs, 1- or 4-H), 4.20 & 4.22(2 x q, J 7Hz, 2 x OCH_2CH_3),
4.42(bs, 4- or 1- H), 5.74 & 6.57(2 x dd, J 6 and 3Hz, 5- and 6-H).

(ii) via Potassium Se,Se-Di(ethoxycarbonyl) Selenosulphate (250).

Potassium sulphite (4.96g, 33.7mmol) and grey selenium (2.29g,
29.0mmol) were heated under reflux in water (50ml) for 30min,
cooled and filtered to give a solution containing potassium
selenosulphate. Diethyl 2-bromomalonate (91) (6.01g, 25.1mmol) in
ethanol (75ml) was added to this solution at room temperature and
the mixture was shaken briefly before addition of cyclopentadiene
(4.00g, 60.6mmol) and calcium chloride dihydrate (3.75g, 25.5mmol)
in ethanol (50ml). Lastly, triethylamine (2.48g, 24.5mmol) in
ethanol (25ml) was added dropwise over 5min with stirring. After a
further 1h stirring at room temperature, the resulting red solution
was evaporated to dryness under reduced pressure with heating. The
residue was dissolved in diethyl ether (50ml) and washed with aq.

hydrochloric acid (50ml) and then water (50ml). The ether layer

was dried (magnesium sulphate), filtered and evaporated to dryness

under reduced pressure to give, after desiccation under vacuum, a

black oil (3.60g). Preparative t.l.c. on silica plates using

ether/light petroleum (3:7) as elutant gave the pure cycloadduct

(230) as a yellow oil (12%). The ^{1}H n.m.r. spectrum of this oil

was identical with that of material made in (i).

Isolation of Diethyl 2,3-Diselenabicyclo[3.3.0]oct-7-ene-4,4- -dicarboxylate (252).

A portion (564mg) of the black oil, containing the cycloadduct

(230), obtained from the selenosulphate (250) as described above,

was left standing at room temperature for about a year before being

purified by preparative t.l.c. on silica plates using

ether/petroleum ether (3:7) as elutant. The cycloadduct (230) was

absent, and the major component isolated was the diselenide (252)

as an orange oil (30.2mg, 2% based on the selenosulphate). [Found:

C, 37.73; H, 4.16%; $\underline{m}/\underline{z}$ (2 x ^{80}Se) 383.9384. $C_{12}H_{16}O_4Se_2$ requires

C, 37.52; H, 4.20%; M^+ (2 x ^{80}Se) 383.9379.]; ν_{max} (thin film)

1740cm^{-1} ; δ_H (200MHz) 1.25(t, $\underline{J}$ 6.9Hz, OCH$_2$C$\underline{H}_3$), 1.26(t, $\underline{J}$ 7.1Hz,

OCH$_2$C$\underline{H}_3$), 2.33(ddq, $\underline{J}_{ex,en}$ 16.9Hz, $\underline{J}_{5,6\alpha}$ 6.4Hz, $\underline{J}_{1,6\alpha}$=$\underline{J}_{7,6\alpha}$=$\underline{J}_{8,6\alpha}$

2.4Hz, 6_{ex}-H), 2.52(ddtd, $\underline{J}_{ex,en}$ 16.9Hz, $\underline{J}_{7,6en}$ 8.3Hz, $\underline{J}_{8,6en}$=$\underline{J}_{1,6en}$

2.3Hz, $\underline{J}_{5,6en}$ 0.7Hz, 6_{en}-H), $\underline{ca}$.4.1-4.4(obscured, 5-H), 4.22(q, $\underline{J}$

7.1Hz, OC$\underline{H}_2$CH$_3$), 4.25(q, $\underline{J}$ 7.2Hz, OC$\underline{H}_2$CH$_3$), 5.09(d, $\underline{J}_{5,1}$ 7.1Hz,

1-H), 5.71 & 5.84(m, 7- and 8-H); δ_c (DEPT 50.3MHz) 13.9 & 14.1(2 x

OCH$_2\underline{C}$H$_3$), 36.7(C-6), 53.4(C-5), 59.7(C-4), 60.8(C-1), 62.3 & 63.0(2

x O$\underline{C}$H$_2$CH$_3$), 129.6 & 133.3(C-7,8), 167.6 & 168.3(2 x CO$_2$).

REFERENCES.

1.   F. Duus in "Comprehensive Organic Chemistry", ed. D. H. R. Barton

     and W. D. Ollis, Vol. 3, p373 (Pergamon 1979).

2.   E. Campaigne in "The Chemistry of the Carbonyl Group", ed. S.

     Patai, Vol. 1, p936 (Wiley-Interscience, 1966).

3.   R. Mayer in "Organosulphur Chemistry", ed. M. J. Janssen, p219

     (Wiley-Interscience, 1967).

4.   R. Mayer, J. Morgenstern, J. Fabian, Angew. Chem. (Ger.), 3, 157,

     (1964).

5.   A. Wagner in "Methoden der Organische Chemie", ed. E. Millar, Vol.

     9, p699 (Verlag, 1955).

6.   E. Campaigne, Chem. Rev., 39, 1 (1946).

7.   A. Ohno in "Organic Chemistry of Sulfur", ed S. Oae, p189 (Plenum,

     1977).

8.   D. Paquer, Int. J. Sulfur Chem. (B), 7, 269 (1972); 8, 173 (1973).

9.   S. M. Weinreb, R. R. Staib, Tet., 3087 (1982).

10. W. Walter, J. Voss in "The Chemistry of the Amide Group", ed J.

     Zabichez, p383 (Wiley-Interscience, 1970).

11. S. Scheithauer, R. Mayer in "Topics in Sulfur Chemistry", ed. A.

     Senning, Vol. 4 (Thieme, 1979).
          S. W. BARANOV, T. E. GORIZO RA AND I. O. KOMARTIA,
12. A. P. Grischchuk Yet al, Chem. Abs., 67, 116869c (1967).
          F. MARSCHNER, K. PRAEFKE, AND P. WEYERSTM-
13. G. Hohne Yet al, Chem. Ber., 108, 673 (1975).

14. C. M. Bladon, I. E. G. Ferguson, G. W. Kirby, A. W. Lochead, D. C.

     McDougall, J. Chem. Soc. Chem. Comm., 423 (1983).

15. G. W. Kirby, A. W. Lochead, J. Chem. Soc. Chem. Comm., 1325 (1983);

G. W. Kirby, A. W. Lochead, G. W. Sheldrake, ibid., 922, 1169 (1984).

16. C. M. Bladon, I. E. G. Ferguson, G. W. Kirby, A. W. Lochead, D. C. McDougall, J. Chem. Soc. Perkin Trans. 1, 1541 (1985).

17. K. Okuma, Y. Komiga, H. Ohta, Chem. Lett., 1145 (1988).

18. H. Staudinger, H. Fraudenberger, Chem. Ber., 61B, 1176 (1928).

19. D. C. Sen, J. Indian Chem. Soc., 12, 647, 751 (1935).

20. A. W. Hofmann, Ann., 145, 360 (1868).

21. A. W. Hofmann, Chem. Ber., 2, 152 (1869); T. Poleck, K. Thummel, ibid., 22, 2871 (1889).

22. R. Mayer, H. Berthold, Chem. Ber., 96, 3096 (1963); R. M. Olofson et al, J. Org. Chem., 29, 1355 (1964).

23. S. O. Lawésson et al, Org. Synth., 62, 158 (1984) and references therein.

24. Badische Anil-u Sodafabuk, German Patent no. 3,8074, (1886).

25. E. Klingsberg, D. Papa, J. Am. Chem. Soc., 73, 4988 (1951); J. Voss, Ann., 746, 92 (1971); D. H. R. Barton, Chem. Abs., 87, 53490n (1977); P. Beslin et al, Tet., 37, 3839 (1981).

26. S. Raucher, P. Klein, J. Org. Chem., 46, 3558 (1981).

27. H. Alper, J. K. Currie, R. Sachdeva, Angew. Chem. Int. Ed. Engl., 17, 689 (1978); A. R. Lapucha, Synthesis, 3, 256 (1987).

28. J. E. Baldwin, R. C. Lopez, Tet, 39, 1487 (1983).

29. K. Beelitz, G. Hohne, K. Praefcke, Z. Naturforsche B., 33, 417 (1978).

30. Prof. J. K. Sutherland, Department of Chemistry, University of Machester, personal communication (1986).

31. E. Vedejs, D. A. Perry, J. Am. Chem. Soc., 105, 1683 (1983).

32. J. C. Powers, F. H. Westheimer, J. Am. Chem. Soc., 82, 5431 (1960).

33. J. Hamer, J. A. Turner in "1,4- Cycloaddition Reactions", ed. J. Hamer, Ch. 8 (Academic Press).

34. E. Vedejs, D. A. Perry, K. N. Houk, N. G. Rondan, J. Am. Chem. Soc., 105, 6999 (1983).

35. D. M. Vyas, G. W. Hay, J. Chem. Soc. Perkin Trans. 1, 180 (1975).

36. E. Vedejs, T. H. Eberlein, R. G. Wilde, J. Am. Chem. Soc., 2220 (1988).

37. B. B. Snider, H. J. Hrib, L. Fuzesi, J. Chem. Soc., 98, 7115 (1976).

38. Arnold, Veeravagne, J. Am. Chem. Soc., 82, 5411 (1960); Gill, Wallace, J. Chem. Soc., Chem. Comm., 380, 382 (1977).

39. G. W. Kirby, S. S.-M. Choi, J. Chem. Soc. Chem. Comm., 177 (1988).

40. G. El. Nagaar, G. W. Kirby, Department of Chemistry, University of Glasgow, personnal communication (1986).

41. A. I. Vogel in "A Textbook of Practical Organic Chemistry.", 3rd. ed., p499 (Longmans, 1986).

42. cf. C. S. Palmer, P. W. McWherter, Organic Synthesis, Collective Volume 1.

43. G. W. Kirby, M. C. McGuire, Department of Chemistry, University of Glasgow, personnal communication (1986).

44.   A. P. Cracknell in "Ultrasonics.", p180 (Wykeham Publications, 1980).

45.   J. Sauer, D. Lang, A. Mielert, Angew. Chem. (Ger.), 74, 352 (1962).

46.   cf. P. Horsewood, G. W. Kirby, R. P. Sharma, J. G. Sweeney, J. Chem. Soc., Perkin Trans. 1, 1802 (1981).

47.   G. W. Kirby, M. S. Rahman, Department of Chemistry, University of Glasgow, personnal communication (1989).

48.   I Fleming in "Frontier Molecular Orbitals and Organic Chemical Reactions.", p164 (Wiley-Interscience, 1976).

49.   E. Block et-al, Angew. Chem. Int. Ed. Engl., 15, 383 (1976).

50.   J. F. King, T. Durst, J. Am. Chem. Soc., 85, 2676 (1963); B. Zwanenburg, J. Strating, Quart. Rep. Sulfur Chem., 5, 79 (1970).

51.   I. W. J. Still, D. V. Frazer, D. K. T. Hutchison, J. F.Sawyer, Can. J. Chem., 368 (1989).

52.   E. Block in "Organic Sulfur Chemistry.", ed. R. Kh. Freidlina, A. E. Skorova, p15 (Pergamon Press).

53.   B. Zwanenburg, Recl. Trav. Chim. Pays-Bas, 101, 1 (1982).

54.   W. Sundermeyer, Synthesis, 349 (1988).

55.   B. Zwanenburg in "Reviews on Heteroatom Chemistry", ed. S. Oae, Vol. 1, p219 (MYU Tokyo, 1989).

56.   W. Walter, G.Randau, Ann. Chem., 681, 55 (1965); W. Walter, K. D. Bode, ibid., 231 (1982).

57.   R. Ammon. H. Berninger, H. J. Haas, I. Landsberg, Arzneum. Forsch., 17, 521 (1967); A. L. Hunter, M. A. Holscher, R. A. Neal, J.

Pharmacol. Exp. Ther., 200, 439 (1977).

58.   B. Zwanenburg, L. Thijs, J. Strating, Tet. Lett., 21, 2871 (1968).

59.   P. Metzner, T. N. Pham, J. Chem. Soc., Chem. Comm., 390 (1988).

60.   B. G. Lenz, H. Regling, H. L. M. van Rozendaal, J. Org. Chem., 50, 2930 (1985).

61.   A. A. Freer, G. W. Kirby, R. A. Lewis, J. Chem. Soc., Chem. Comm., 718 (1987).

62.   W. A. Sheppard, J. Dieckmann, J. Am. Chem. Soc., 86, 1891 (1964).

63.   T. Back, D. Barton, M. Britten-Kelly, F. Guziec, J. Chem. Soc., Perkin Trans. 1, 3, 2079 (1976).

64.   N. Ramnath et al, Chem. Lett., 89 (1982).

65.   E. Wederkind, D. Schenk, R. Stusser, Ber., 56, 633 (1923).

66.   J. F. King, T. Durst, Tet. Lett., 585 (1963).

67.   J. Strating, Recl. Trav. Chim. Pays-Bas, 83, 94 (1964); J. F. King, Acc. Chem. Res., 8, 10 (1975).

68.   W. Walter, Ann, 633, 35 (1960).

69.   W. Wilkens, Ph.D. Thesis, Cornell University, Ithaca N. Y. (1961); A. I. Virstanen, Angew. Chem, 74, 374, (1962).

70.   A. Elsasser, W. Sundermeyer, Chem. Ber., 118, 4553 (1985).

71.   W. J. Middleton, E. G. Howard, W. H. Sharkey, J. Org. Chem., 30, 1384 (1985); T. Kitazume, N. Ishikawa, Chem. Lett., 267 (1973).

72.   E. Block, A. Wall, J. Org. Chem., 52, 809 (1987).

73.   H. L. M. van Rozendaal, B. Zwanenburg, J. Org. Chem., 50, 2930 (1985).

74.   R. W. Saalfrank, W. Rost, Angew. Chem. Int. Ed. Engl., 24, 855 (1985).

75.   E. Block, A. A. Bazzi, L. K. Revelle, J. Am. Chem. Soc., 102, 2490 (1980).

76.   S. S. Battacharjee, H. Ila. Junjappa, Sythesis, 249 (1984).

77.   I. W. J. Still, F. J. Ablenos, J. Chem. Soc., Chem. Comm., 542 (1985).

78.   J. A. M. KUIPERS, B. H.M. LAMBRINK, I.W.J. STILL, AND B. Zwanenburg et al, Synthesis, 295 (1981).

79.   A. G. Schultz, R. H. Schlessinger, J. Chem. Soc., Chem. Comm, 747, 748 (1970).

80.   G. E. Veentra, B. Zwanenburg, Tet, 34, 1585 (1978).

81.   G. E. Veentra, B. Zwanenburg, Recl. Trav. Chim. Pays-Bas, 95, 28 (1976).

82.   E. Flood, J. E. Boggs, J. Mol. Struct., 34, 147 (1976).

83.   J. P. Snyder, J. Org. Chem., 38, 3965 (1973); I. Fleming in "Frontier Orbitals and Organic Chemical Reactions.", p147 (Wiley-Interscience, 1976).

84.   A. I. Vogel in "A Textbook of Practical Organic Chemistry.", 3rd. ed., p303 (Longmans, 1986).

85.   M. E. Jung, C. A. McCombs, Tet. Lett., 2935 (1976).

86.   cf. E. Juaristi, J. S. Cruz-Sanchez, A. Peterson, R. S. Glass, Tet., 44, 5653 (1988) and references therein.

87.   A. J. Kirby in "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen.", p31 (Verlag, 1983).

88.   W. H. H. Gunther in "Organic Selenium Compounds: Their Chemistry

        and Biology.", ed. D. L. Klayman and W. H. H. Gunther, p59 (Wiley-

        -Interscience, 1973); R. B. Silverman, ibid., p245; K. A. Jenson,

        ibid., p263; K. G. Mautner, ibid., p473.

89.   K. J. Irgolic, M. V. Kudchadker in "Selenium.", ed. R. A. Zingaro

        and W. C. Cooper (Van Nostrand Reinhold, 1974).

90.   "Organic Compounds of Sulphur, Selenium and Tellurium.", vols. 1-6,

        (Specialist Periodical Reports; The Chemical Society: London,

        1970-81).

91.   C. Paulmier in "Selenium Reagents and Intermediates in Organic

        Synthesis.", ed. J. E. Baldwin, p58 (Pergamon Press, 1986).

92.   F. J. Guziec Jnr. in "Organoselenium Chemistry.", ed. D. Liotta,

        p277 (Wiley-Interscience, 1987).

93.   T. C. Wong, F. J. Guziec Jnr., C. A. Moustakis, J. Chem. Soc.,

        Perkin Trans. 2, 1471 (1983).

94.   H. E. Hallen, C. M. Jones, J. Chem. Soc. (A), 1033 (1969).

95.   I. D. Rae, M. J. Wade, Int. J. Sulphur Chem., 8, 519 (1976).

96.   C. D. Mickey, R. A. Zingaro, ibid., 8, 557 (1976).

97.   P. T. Meinke, G. A. Krafft, Tet. Lett., 28, 5121 (1987).

98.   J. Nakajama, K. Akimoto, J. Niijima, M. Hoshino, Tet. Lett., 28,

        4423 (1987).

99.   G. W. Kirby, A. N. Tretheway, J. Chem. Soc., Perkin Trans. 1, 1913

        (1988).
                J. SAKIATA, Y.TACHIBAZR, T.HOWOA AND H.OHTA.
100.   K. Okuma et al., Tet. Lett., 6649 (1987); Chem. Lett., 1145
                                                        K.OKUMA, Y.KOMIYA AND H.OHTA.

(1988).

101.   T. Back, D. Barton, M. britten-Kelly, F. J. Guziec Jnr., <u>J. Chem.</u>

        <u>Soc., Chem. Comm.</u>, 539 (1975); <u>J. Chem. Soc., Perkin Trans. 1</u>, <u>3</u>,

        2079 (1976).

102.   T. W. Campbell, H. G. Walker, G. M. Cappinger, <u>Chem. Rev.</u>, <u>50</u>, 279

        (1952).

103.   D. S. Margolis, R. W. Pittman, <u>J. Chem. Soc.</u>, 799 (1957).

104.   W. H. H. Gunther in "Organic Selenium Compounds: Their Chemistry

        and Biology.", ed. D. L. Klayman and W. H. H. Gunther, p35 (Wiley-

        -Interscience, 1973).

105.   ibid., p45

106.   A. A. Kudryavtsev in The Chemistry and Technology of Selenium.",

        p57 (Collet's, 1974).

107.   H. Grimm, H. Metzner, <u>Ber.</u>, <u>69B</u>, 1356 (1936).

108.   W. H. H. Gunther in "Organic Selenium Compounds: Their Chemistry

        and Biology.", ed. D. L. Klayman and W. H. H. Gunther, p44 (Wiley-

        -Interscience, 1973).

109.   R. Okazaki, A. Ishii, N. Inamoto, <u>J. Chem. Soc., Chem. Comm.</u>, 1429

        (1983).

110.   cf. F. J. Moustakis, C. A. Moustakis, <u>J. Org. Chem.</u>, <u>49</u>, 189

        (1984); R. Okazaki, K. Inoue, N. Inamoto, <u>Tet. Lett.</u>, 3673 (1979).

111.   G. E. Erker, R. Hock, <u>Angew. Chem. Int. Ed. Engl.</u>, <u>28</u>, 179 (1989).

112.   K. Steliou, M. Mrani, <u>J. Am. Chem. Soc.</u>, <u>104</u>, 3104 (1982).

113.   M. Segi T. NAKASIMA, S. SUGA, S. MURAI, I. RYU, A. OGAWA AND N. SONADA, <u>J. Am. Chem. Soc.</u>, <u>110</u>, 1976 (1988).

114.   J. GALLON, W. H. WATSON, D. CRAIG, C. GUIDRY, R. M'KELLAR,
       AND A. L. TERNAY, JNR., J. Heterocyclic Chem., 20, 399 (1983).

115.   C-P. Klages, J. Voss, Angew. Chem. Int. Ed. Engl., 16, 725 (1977).

116.   G. Traverso, Ann. Chim. (Rome), 47, 3 (1957).

117.   K. NAKAMURA, M. UOHAMA, S. OKA, T. YAMABE, AND S. NAGATA,
       A. Ohno et al, Bull. Chem. Soc. Jpn., 48, 3718 (1975).

118.   P. de Mayo, G. L. R. Patrasiumas, A. C. Weedon, Tet. Lett., 4621

       (1978).

119.   G. W. Kirby, G. M. A. Naggar, personal communication, 1986.

120.   J. G. Stark, H. G. Wallace in "Chemistry Data Book.", 2nd ed., p13

       (John Murray, 1982).

121.   G. W. Kirby, A. N. Tretheway, personal communication, 1988.

122.   J. Sauer, D. Lang, A. Mielert, Angew. Chem., 74, 352 (1962).

123.   cf. R. C. Brown in "Pyrolytic Methods in Organic

       Chemistry: Applications of Flow and Flash Vacuum Pyrolysis

       Techniques." (Academic Press, 1980).