SOME ASPECTS OF ARSONIUM YLIDE CHEMISTRY

by

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FOR MY
PARENTS -
GRATITUDE
IS NOT
ENOUGH

DECLARATION

I declare that this thesis is my own composition, that the work of which it is a record has been carried out by myself, and that it has not been submitted in any previous application for a higher degree.

The thesis describes results of research carried out in the Department of Chemistry, University of Edinburgh, under the supervision of Dr. I. Gosney since the 1st October 1977, the date of my admission as a research student.

The following courses were attended during the three years of research:

Lab. 29 seminars (three years attendance); "Chemistry at its most Colourful", 5 lectures by Staff of I.C.I. Organics Division, Blackley; "Basic and Advanced Stereochemistry", 5 lectures by Dr. H. McNab (University of Edinburgh); "Strategy of Organic Synthesis", 5 lectures by Dr. I. Gosney (University of Edinburgh); "The Bio-organic Chemistry of Drugs, Toxins and other Xenobiotics", 5 lectures by Dr. A.G. Rowley (University of Edinburgh); "Organic Electrochemistry", 5 lectures by Dr. A.J. Bellamy (University of Edinburgh); "Flash Vacuum Pyrolysis", 5 lectures by Dr. H. McNab (University of Edinburgh).

19/5/81

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ABSTRACT

The preparation of a series of 4*H*-1,3-thiazines is described. The preparation studies have involved the reaction of *N*-substituted-3-isothiazolones with both arsonium ylides and with carbenoid species.

The reaction of triphenylarsonium phenacylide with propiolic esters has been found to provide a route to a novel class of ars(V)oranes. The same reaction does not occur with the corresponding carbomethoxymethylide or with phosphonium ylides. A mechanism is postulated for the reaction.

The effect of solvent on the reaction of arsonium ylides with benzaldehyde has been studied. The ratio of epoxide/olefin is found to be solvent dependent and a possible rationale is put forward.

CONTENTS

1. Introduction

1.1 Preamble

An ylide can be defined as a substance in which a carbanion is attached directly to a heteroatom carrying a high degree of positive charge, but this structure (1a) may, in resonance terms, be only one of several forms contributing to the overall structure of the molecule. Although the nature of the heteroatom can vary widely, $\overset{+}{X}$ is usually an ammonium ($-\overset{+}{N}R_3$), phosphonium ($-\overset{+}{P}R_3$), arsonium ($A\overset{+}{s}R_3$), or sulphonium ($-S^{+}R_2$) group

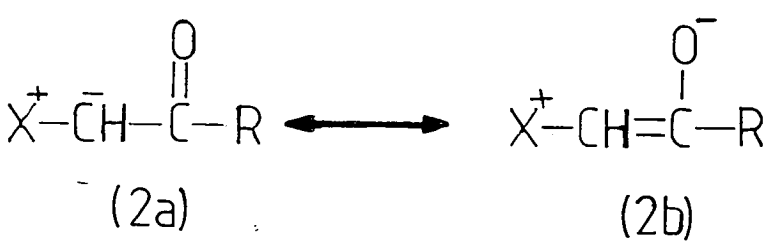
(1a) (1b)

The nature of the C-X bonding can be described in terms of pπ-dπ overlap in the apolar form as implied by the canonical form (1b), although coulombic stabilisation will play an important part, especially for nitrogen ylides. The resonance structure (1b) is used to imply delocalisation of the carbanion electrons into the vacant orbitals of the heteroatom. The contribution to the overall structure of the ylide of structure (1b) depends very much on the ability of the heteroatom to expand its octet, and the effectiveness of the resulting pπ-dπ overlap.

An alternative description of ylides invokes hypervalent bonding, whereupon an ylide is considered as a hypervalent molecule in which a 3-centre bond is

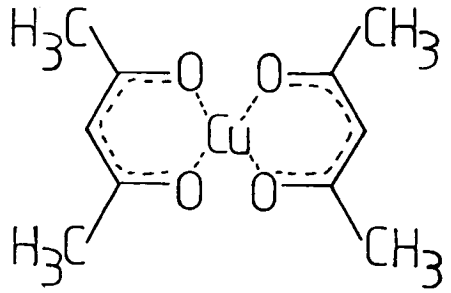
reduced to a 2-centre bond using a single orbital from the hypervalent atom and formally transferring one electron from the main group atom to the ylide carbon or nitrogen[1].

Ylides may vary widely in stability, depending on the ability of the positively charged heteroatom to stabilise the negative charge by inductive and mesomeric action e.g. (1a) ↔ (1b). Stabilisation can also be provided by the presence of a conjugating group attached to the carbanionic centre, presumably because the negative charge in the dipolar form can be delocalised into the group e.g. the carbonyl group, (2a) ↔ (2b). The term "stabilised ylide" is used in general to describe an ylide that can be isolated, purified by recrystallisation, and stored in the atmosphere for use in a subsequent experiment. Such ylides usually bear strongly electron-withdrawing groups on the carbanion carbon adjacent to the heteroatom.



(2a) (2b)

The special characteristic of ylides that makes them worthy of study in their own right is the unique stabilisation afforded to carbanions by the presence of the adjacent heteronium group. Many ylides have been isolated as stable substances whereas normal carbanions are seldom isolable unless strongly stabilised by adjacent acyl groups, e.g. copper acetylacetonate (3).



(3)

Although the first reported ylide, triphenylphosphonium carboethoxymethylide, was isolated by Michaelis and Gimborn[2] in 1894 it was not until the 1950's that Wittig and co-workers[3] established ylides as useful synthetic intermediates. Wittig's group showed that triphenylphosphonium methylide (4, X = PH_3P, R = CH_2) and its derivatives were useful as olefin forming reagents (Scheme One). This reaction is now universally known as the Wittig reaction.

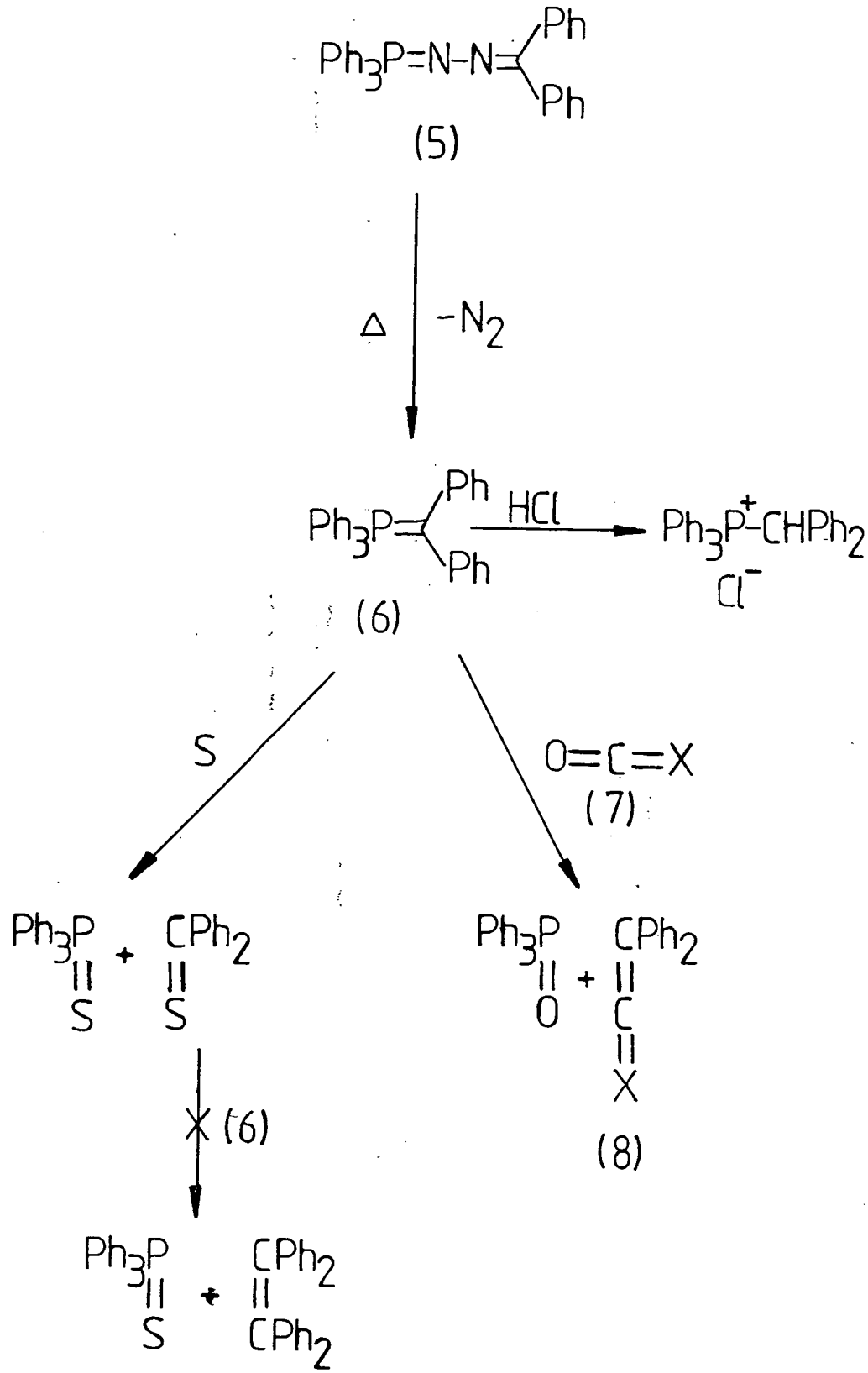
(4)

X = heteroatom group

R = hydrocarbon group

Scheme One

The reaction between triarylphosphonium alkylides and carbonyl compounds has proved to be, because of its specificity and good yields, widely applicable for the conversion of carbonyl compounds into their olefinic entities[3,4]. It is almost entirely due to this aspect of their use that there has been such an enormous

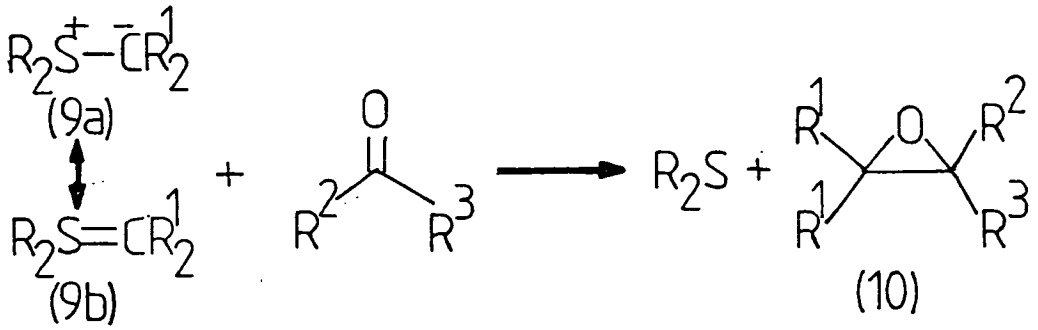

Ph3P=N-N=C(Ph)Ph
(5)
Δ
-N2
Ph3P=C(Ph)Ph
(6)
HCl
Ph3P+-CHPh2
Cl-
S
O=C=X
(7)
Ph3P=S + CPh2=S
X (6)
Ph3P=S + CPh2=CPh2
Ph3P=O + C(=X)
(8)

Scheme Two

interest in the chemistry of ylides over the last twenty five years.

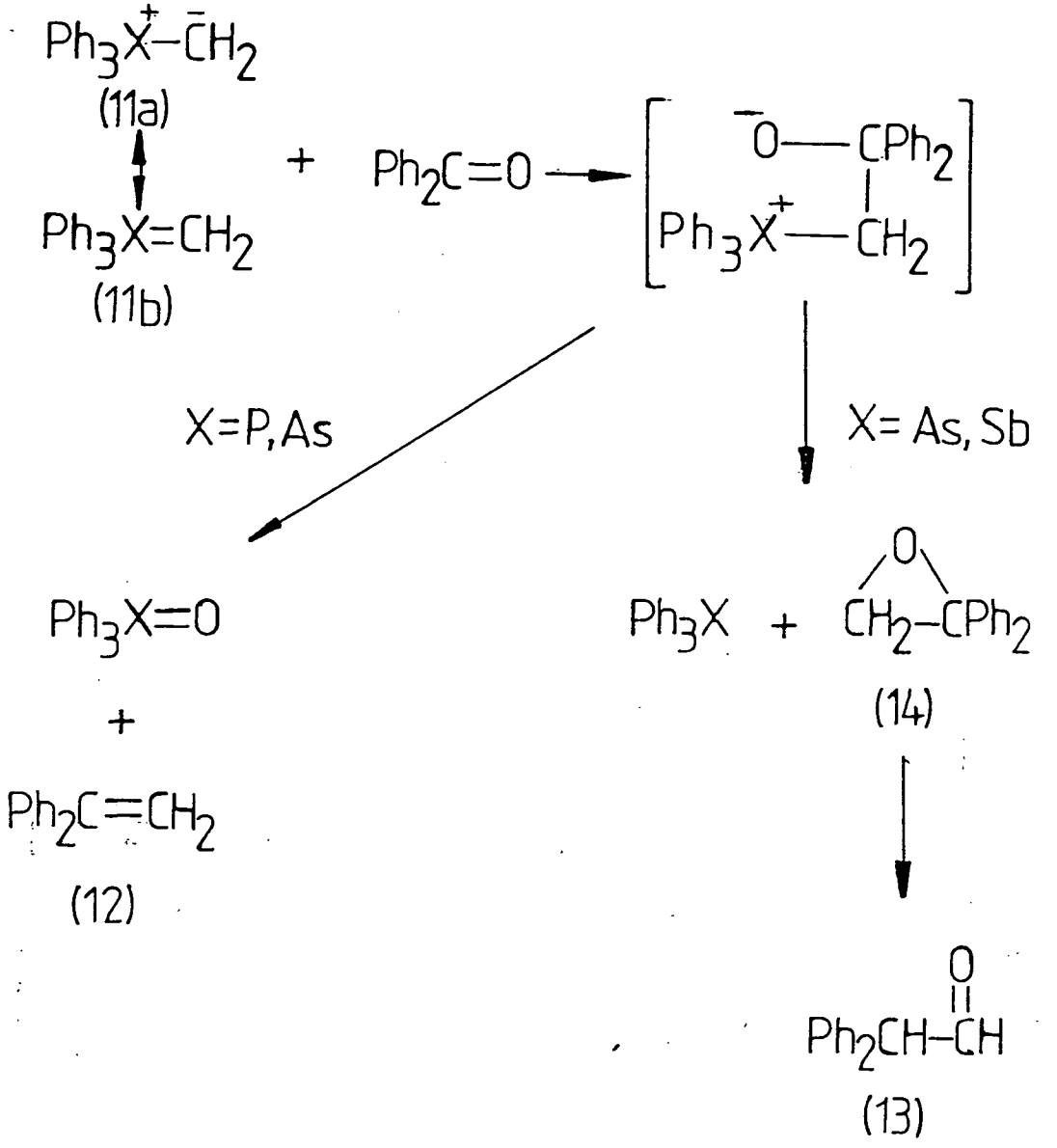
It is of interest to note that prior to the work of Wittig, Staudinger and Meyer[5] isolated triphenylphosphonium diphenylmethylide (6) from the decomposition of the corresponding phosphinazine (5), but due to the stability of the ylide they could only obtain products from reaction with very reactive carbonyl compounds, e.g. diphenylketene (7; X = CPh_2) and phenylisocyanate (7; X = NPh) (Scheme Two).

Concurrent with the development of phosphonium ylide chemistry has been the slower but equally spectacular evolution of sulphonium ylide chemistry[6]. This was due initially to the work of Johnson and co-workers[7], and of late by Trost[6] and Ando[8]. What makes sulphonium ylides important is that they afford a useful method for the direct synthesis of epoxides from carbonyl compounds, without the intermediate formation of olefins (Scheme Three).

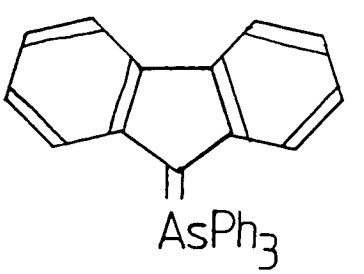


Scheme Three

Wittig and Henry[9] extended the Wittig reaction to ylides of other group 5A elements (11, X = As, Sb). Whereas triphenylphosphonium methylide (11, X = P)

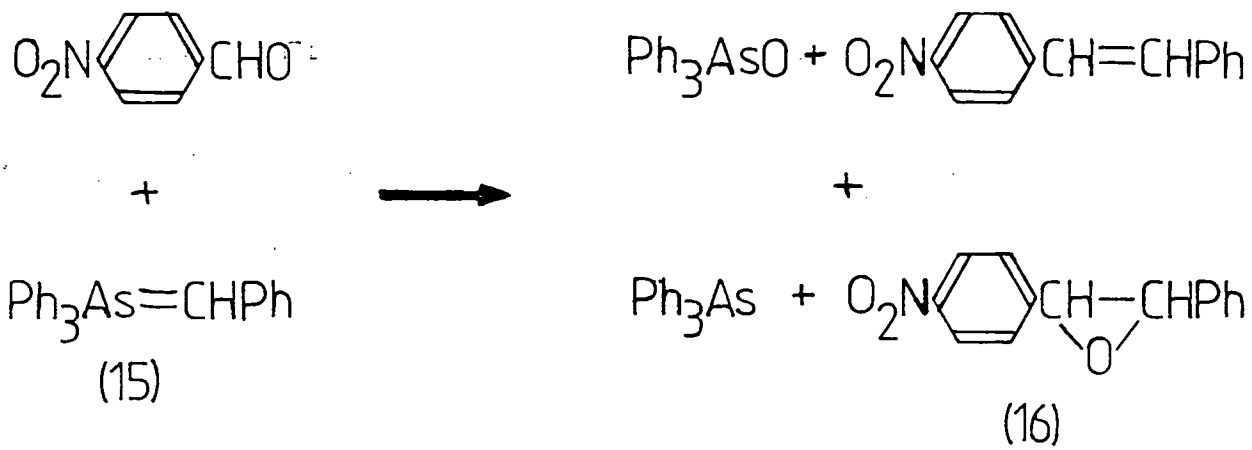


Scheme Four



(17)

and benzophenone afforded the olefinic compound (12), reaction with triphenylarsonium methylide (11, X = As) gave the corresponding aldehyde (13) as the major product together with minor amounts of olefin (12). A similar reaction with triphenylstibonium methylide (11, X = Sb) gave the corresponding aldehyde exclusively (Scheme Four). To explain this surprising result, Wittig proposed that the aldehyde (13) was formed <u>via</u> the epoxide (14), probably by an acid catalysed rearrangement during the workup. However no proof was available for this mechanism until Johnson and Martin[10] isolated the epoxide (16) from the reaction between triphenylarsonium benzylide (15) and <u>p</u>-nitrobenzaldehyde (Scheme Five).



Scheme Five

Reaction of the stabilized ylide, triphenylarsonium fluorenylide (17) with aldehydes afforded only alkenes[11]. Subsequent work has shown that stabilised arsonium ylides react with aldehydes to give olefins[12]. Hence the early work on arsonium ylides in their reaction with carbonyl compounds suggested that arsenic seems to lie between

sulphur and phosphorus in its effect on the properties of ylides. This dual nature of arsonium ylides in the Wittig reaction and their general enhanced reactivity compared to their phosphonium and sulphonium analogues has led to an upsurge in their chemistry.

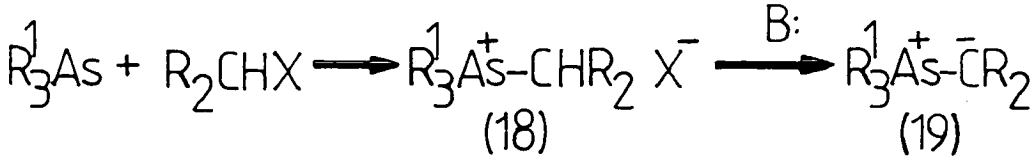
This thesis is concerned with the utility of arsonium ylides in heterocyclic synthesis. Gaudiano has used arsonium ylides in the preparation of indoles[13], Δ^2-isoxazolines[14] and 5-hydroxyisoxazolines[15]. The target heterocyclic molecules in this study were the relatively unexplored 1,3-thiazines. Such compounds are of interest not only for their therapeutic activity, but also because of the presence of a 1,3-thiazine as part of the basic ring structure present in cephalosporins. As most of the work in this present study has been concerned with aspects of the chemistry of arsonium ylides, the introduction which follows will describe their preparation and properties in detail.

1.2 Methods of synthesis of arsonium ylides

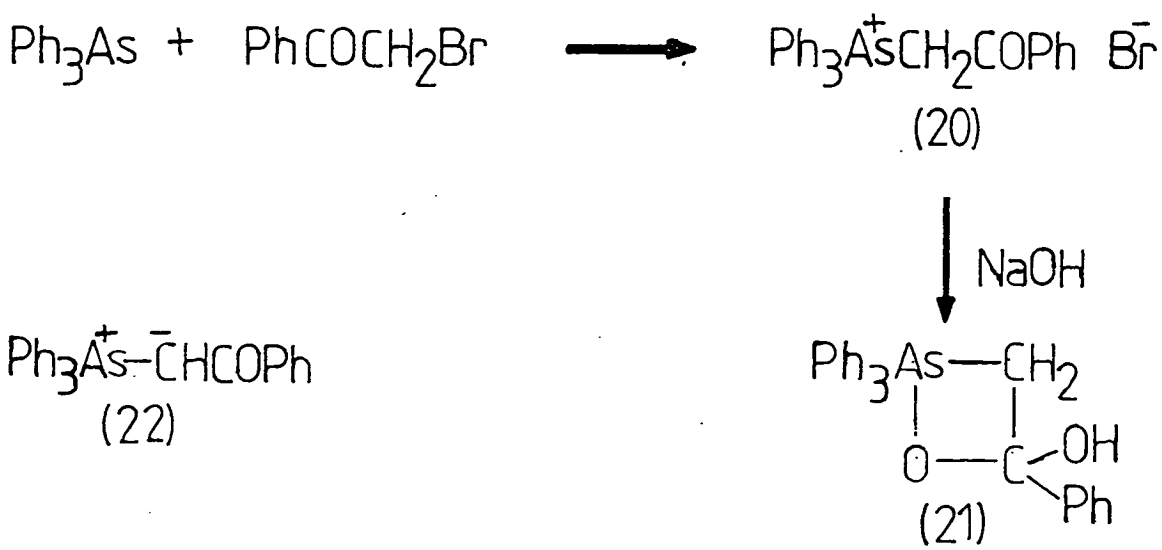
Several methods exist for the preparation of ylides in general including the salt method, the diazo method, condensation methods and transylidation. In principle there is no reason why any method applicable to the synthesis of phosphonium (or for that matter sulphonium) ylides cannot be adopted for the synthesis of arsonium ylides.

1.2.1 Salt method

Most arsonium ylides to date have been obtained by the so-called 'salt method'. The usual procedure involves the reaction of an arsine with an alkylhalide to give an arsonium salt (18) which on treatment with base affords the ylide (19) by removal of an α-hydrogen.



The first preparation of an arsonium ylide in this way was due to Michaelis[16] who found that phenacyltriphenylarsonium bromide (20) upon addition of sodium hydroxide gave a substance which he formulated as the betaine structure (21) (Scheme Six). It was not until the 1950's that Krohnke[17] correctly identified the product as triphenylarsonium phenacylide (22). Several years later Nesmeyanov[18] reported the preparation of several other β-ketoarsonium ylides by the same route.



Scheme Six

Generally, stabilised arsonium ylides can be generated by the salt method in aqueous media. This is due to the acidity afforded the α-hydrogen by the stabilising groups. Reactive ylides must be generated under anhydrous conditions by a strong base, e.g. butyllithium, because the resulting ylide is not stabilised by electron withdrawing groups on the carbanion carbon.

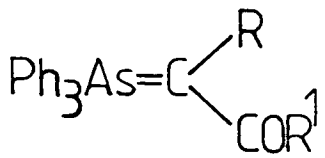
Krohnke[17] also investigated the reactions of o-, m-, and p-nitrobenzyltriphenylarsonium salts with aqueous alkali and ascribed the coloured solutions obtained to the generated ylides. He also attributed the marked increase in colour intensity of the o- and p-isomers compared with the m-isomer to resonance interactions of the type (23a) ↔ (23b).

(23a) (23b)

In 1960 Johnson[11] reported the preparation and isolation of triphenylarsonium fluorenylide (17), the first example of an isolable arsenic-containing ylide. Thus, treatment of triphenylarsine with 9-bromofluorene afforded triphenylfluorenylarsonium bromide which, in the presence of aqueous ethanolic sodium hydroxide, gave the ylide as yellow plates in high yield.

Nesmeyanov[18] later prepared and isolated ylides

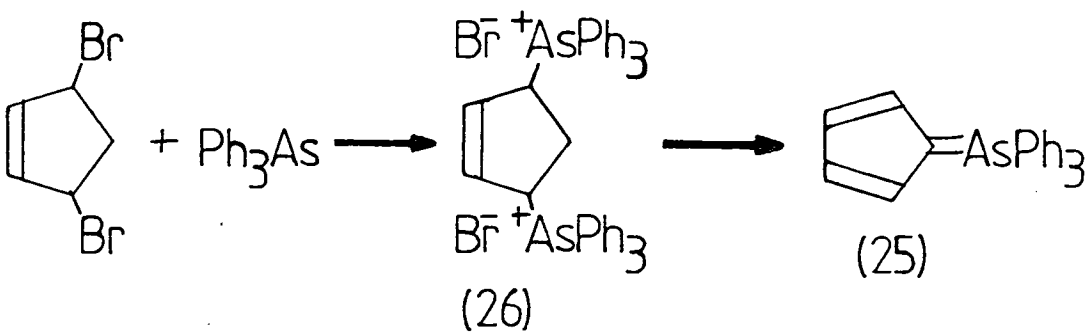
of the type (24). Some Chinese workers[19] independently prepared triphenylarsonium carbomethoxymethylide (24a) by a similar route. These stabilised arsonium ylides were prepared by the action of a variety of bases on arsonium salts derived from triphenylarsine and α-bromoketones.



(24)

24a, R=H, R^1=OMe;
b, R=H, R^1=Me;
c, R=H, R^1=Ph;
d, R=Ph, R^1=OMe;
e, R=H, R^1=NH_2

Interestingly, Nesmeyanov[18] failed to obtain triphenylarsonium cyclopentadienylide (25) by the treatment of a cyclopentadienyltriphenylarsonium salt with base. However, in 1971 Lloyd and Freeman[20] prepared this ylide by keeping a solution of dibromocyclopentene and triphenylarsine at room temperature for ten days and treating the cyclopentene bis-arsonium salt (26) so obtained with aqueous sodium hydroxide. The ylide formed a crystalline perchlorate and dissolved in mineral acid from which it could be precipitated unchanged upon the addition of alkali.



(26) (25)

Froyen has prepared and isolated a series of stabilised arsonium ylides by the salt method[21]. The arsonium salts were made from the respective arsines by treatment with the appropriate α-bromoketones, esters or amides, and the ylides (27) were generated using various bases.

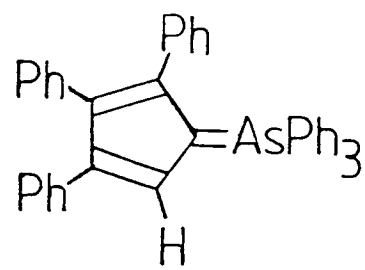
$R_3As{=}CH.COX$

(27)

27 a) R=Ph; X=OMe, NPh_2, Me, p-MeC_6H_4, p-PhC_6H_4, Ph, p-BrC_6H_4, p-$NO_2C_6H_4$.

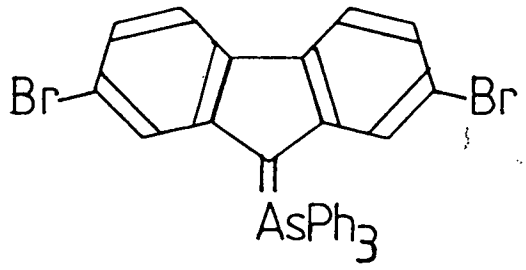
b) X=Ph; R=p-$MeOC_6H_4$, p-MeC_6H_4.

Triphenylarsonium 2,3,4-triphenylcyclopentadienylide (28) has been prepared and isolated by Lloyd and Singer[22] using the salt method.



(28)

Using the salt method, Tewari and Gupta[23] have prepared and isolated triphenylarsonium 2,7-dibromo-9-fluorenylide (29) in 70% yield by refluxing 2,7-dibromo-9-fluorenyltriphenylarsonium bromide with ammonium hydroxide in ethanol.



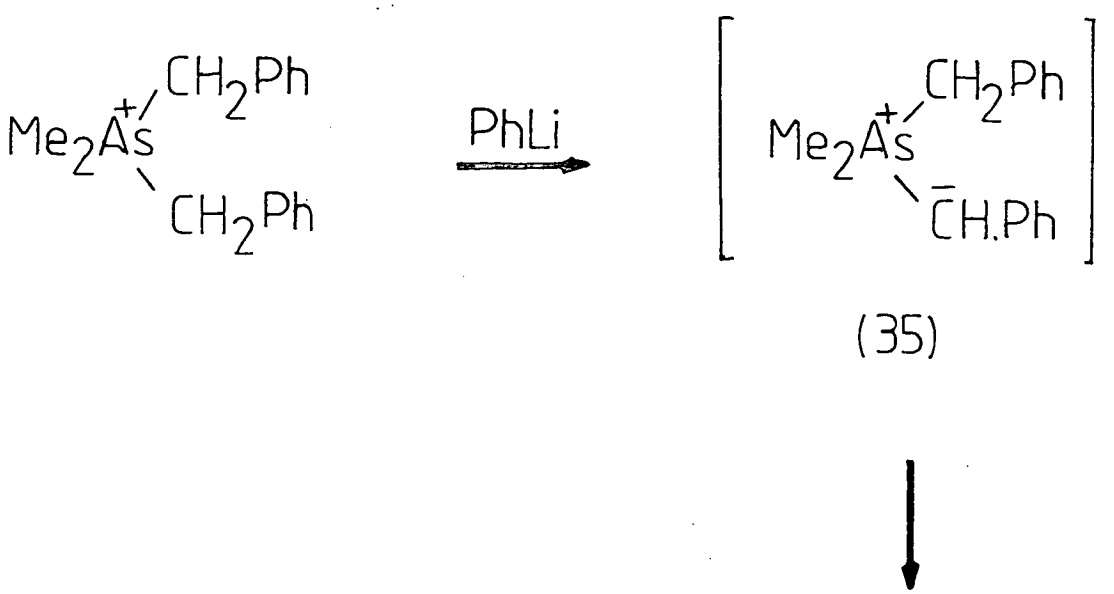
(29)

Unlike stabilised arsonium ylides, reactive ylides are seldom isolated and characterised. Several groups[9,24,25] have independently prepared methyltriphenylarsonium halides by direct alkylation. In all cases, treatment of the ethereal slurry of the arsonium salt with butyllithium gave the ylide, triphenylarsonium methylide (30), but no attempts were made to isolate it. This was eventually achieved by Yamamoto and Schmidbaur[26] who generated the ylide from its hydrobromide in tetrahydrofuran at 20°C by treatment with sodium amide under nitrogen. After filtration under nitrogen, and evaporation <u>in vacuo</u>, the ylide was obtained as yellow needles (m.p. 74°C) from ether.

$$Ph_3\overset{+}{A}s-\bar{C}H_2$$

(30)

Miller[27] has prepared a distillable arsonium ylide, trimethylarsonium trimethylsilylmethylide (31) by the reaction of trimethylarsine with chloromethyltrimethylsilane and subsequent deprotonation of the isolated arsonium salt (32) with butyllithium. The chloride salt



Scheme Seven

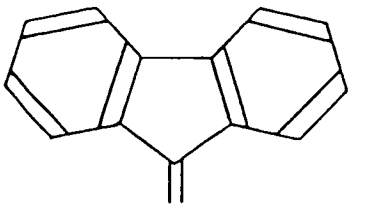
could be regenerated by treatment of the ylide with dry hydrogen chloride. In an extension to this reaction Schmidbaur and Tronich[28] have obtained the simplest ylide, trimethylarsonium methylide (33) by desilylation of (31) with trimethylsilanol. After removal of the hexamethyldisiloxane formed, the ylide (33) was purified by sublimation (30-35°C; 0.1 mmHg) to give colourless crystals (m.p. 33-35°C) which were sensitive to air and moisture.

$Me_3\overset{+}{A}s-\overset{-}{C}H.SiMe_3$ (31)

$Me_3\overset{+}{A}s-CH_2SiMe_3\,Cl^-$ (32)

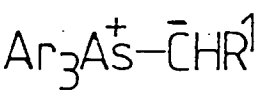
$Me_3As=CH_2$ (33)

Wittig and Laib[29] have prepared solutions of trimethylarsonium fluorenylide (34, X = Me) and benzyldimethylarsonium fluorenylide (34, X = CH_2Ph). However, no attempts were made to isolate and characterise these ylides and they were handled entirely in solution. The parent salts were prepared by alkylation of an arsine with 9-bromofluorene, and the ylides were generated by treatment of the salts with phenyllithium. The authors also attempted to prepare the ylide (35) from dibenzyldimethylarsonium salts but found that, although the ylide had apparently formed as indicated by the appearance of a short lived yellow colour, it changed spontaneously into dimethyl-(1,2-diphenylethyl)arsine (36), apparently <u>via</u> a Stevens rearrangement (Scheme Seven).



(34)

Several other arsonium ylides have been prepared by the salt method but in some cases could not be isolated due to their facile hydrolysis. Walker and Trippett[30] prepared several arsonium ylides (37) in ethanol solution.

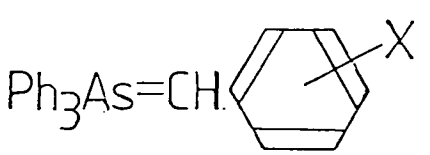


(37)

37 a) Ar=Ph; R^1=Ph, p-ClC_6H_4, p-$NO_2C_6H_4$, p-CNC_6H_4, H, CO_2Et

b) Ar=p-$MeOC_6H_4$; R^1=Ph, p-$NO_2C_6H_4$

As part of their studies into the reaction between semi-stabilised ylides and carbonyl compounds, Tewari and co-workers have prepared several triphenylarsonium substituted-benzylides (38): X = p-NO_2 [31], o-NO_2 [32], m-NO_2 [32], p-Br [33], p-I [33]. The same workers have also prepared triphenylarsonium 2-naphthylmethylide (39, R=H) and triphenylarsonium 1-bromo-2-naphthylmethylide (39, R=Br) in the same way[34].



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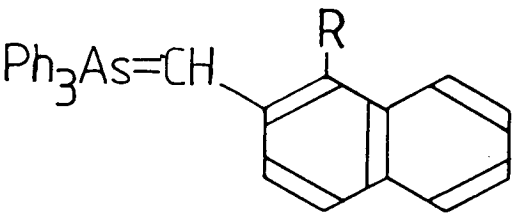
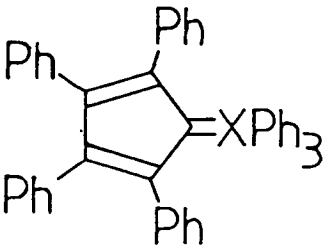


(39)

1.2.2 Diazo method

The diazo method has been used to prepare stabilised arsonium ylides. In 1966, Lloyd and Wasson[35] observed that tetraphenyldiazocyclopentadiene decomposed with evolution of nitrogen on heating above its melting point. When this decomposition was carried out in the presence of triphenylphosphine, the ylide (40) was formed. The formation of (40) was ascribed to the thermal generation of a carbene which reacted with the lone pair of electrons on the heteroatom. Evidence for these proposals was obtained by a thermogravimetric analysis of the reactions between diazotetraphenylcyclopentadiene and a number of substrates containing heteroatoms[36]. The results indicated that they proceeded via a common step which was taken to be the formation of the carbene, tetraphenylcyclopentadienylidene. It is of interest that the reaction between triphenylphosphine and diazotetraphenylcyclopentadiene in boiling p-cymene afforded the phosphinazine adduct (41)



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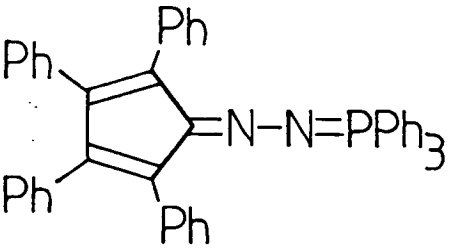
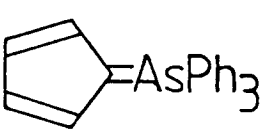


(41)

In later work, Lloyd and co-workers[37] used the carbene method to prepare triphenylarsonium tetraphenylcyclopentadienylide (40) and the parent triphenylarsonium cyclopentadienylide (42). Interestingly, triphenylarsonium 2,3,4-triphenylcyclopentadienylide (43) could not be prepared in this way[22]. The reaction of triphenylphosphine with diazo-2,3,4-triphenylcyclopentadiene gave only the phosphinazine adduct (44)[22].



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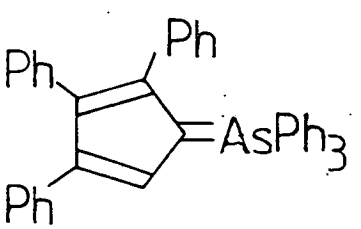

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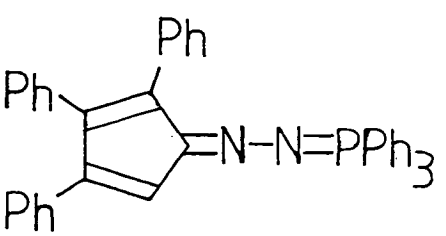

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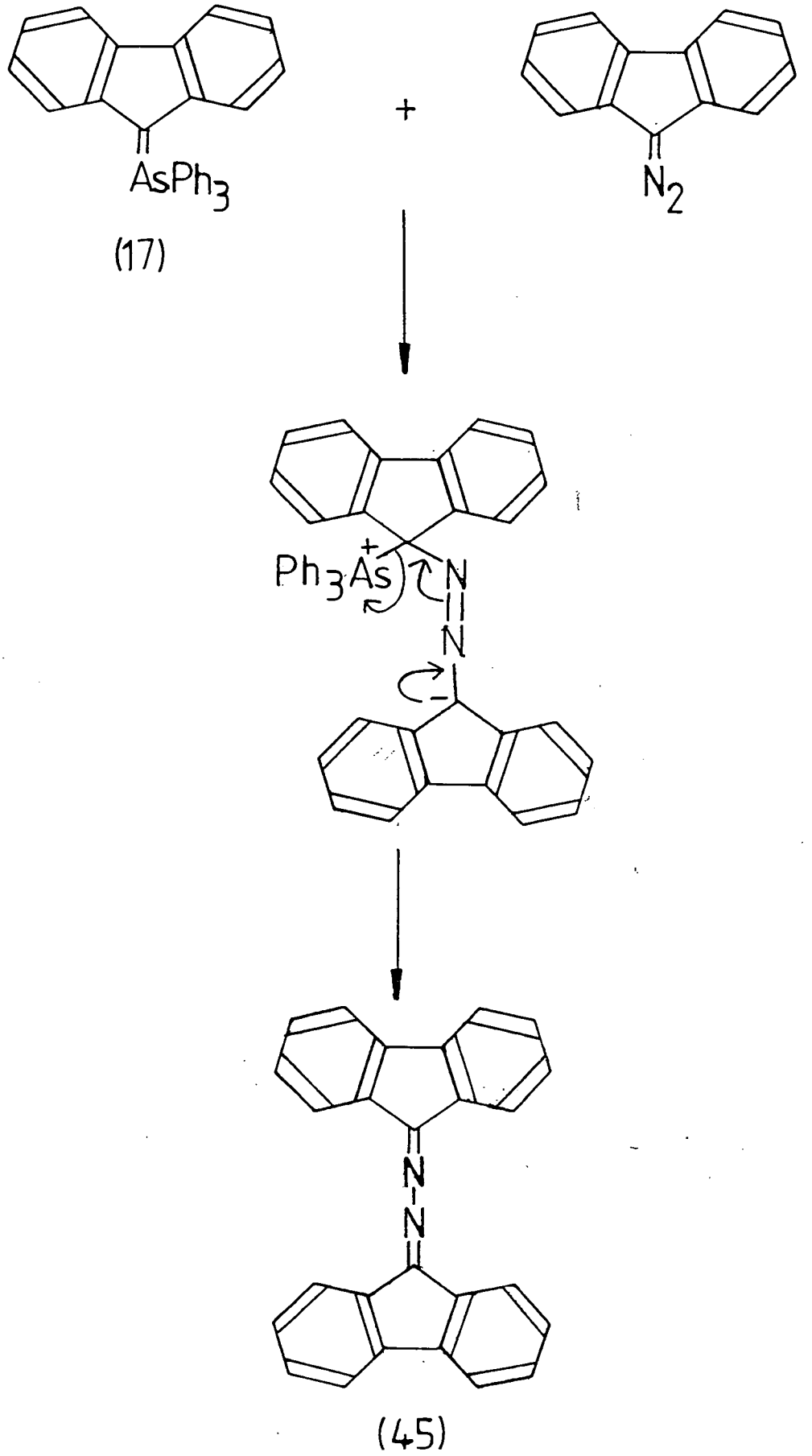


(17)

(45)

Scheme Eight

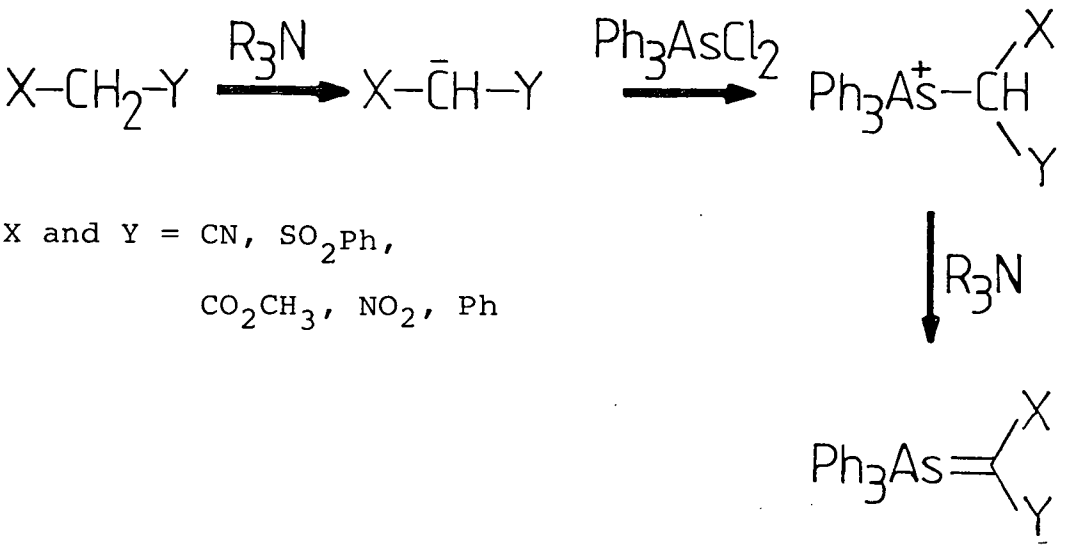
Later, Freeman and Lloyd[20,38] prepared a series of substituted cyclopentadienylarsonium ylides by the carbenic decomposition of the appropriate diazocyclopentadienes in the presence of triphenylarsine. The yields of the ylides were low but could be considerably improved by the addition of copper catalysts to the melt or boiling solution of reactants. This technique was known to generate singlet carbenes or carbenoid species[39].

Gosney and Lloyd[40] have extended the scope of this procedure by employing a variety of diazo compounds. In all cases the compounds carried strongly electron-withdrawing groups and were decomposed in a melt at 150°C in the presence of triphenylarsine and copper catalysts. The functionally disubstituted ylides obtained were stable to the atmosphere and characterised by analysis and spectroscopic properties.

There are some limitations to this method; for example, 9-diazofluorene and triphenylarsine yielded fluorenone ketazine (45) almost quantitatively rather than the expected ylide (17)[40]. Apparently in this instance, further reaction of the ylide occurred with undecomposed diazo compound as shown in Scheme Eight. Evidence for this was obtained by mixing solutions of equimolar quantities of diazofluorene and ylide (17) at room temperature, when essentially quantitative yields of the ketazine (45) and of triphenylarsine were obtained. Similar reactions have been observed with phosphonium[41,42,43] and pyridinium[41] ylides.

1.2.3 Condensation methods

Horner and Oediger[44] have extended their simple method for the synthesis of functionally disubstituted phosphonium ylides to arsonium ylides by reacting triphenylarsine dichloride with active methylene compounds in the presence of triethylamine. The reaction presumably proceeds as shown in Scheme Nine.

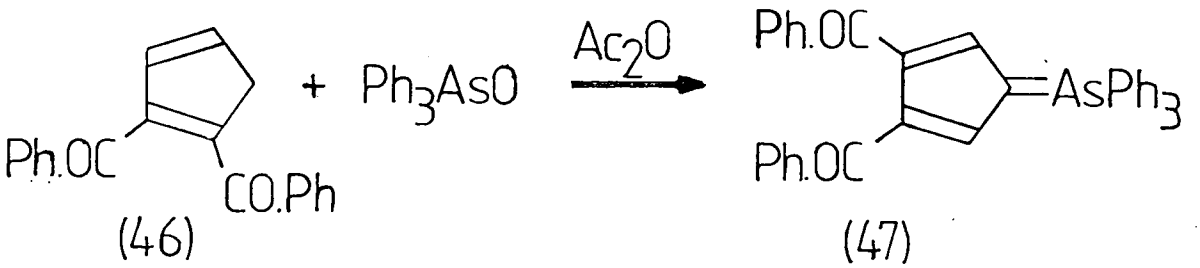


Scheme Nine

However, the method is limited to the preparation of ylides carrying two electron-withdrawing groups, i.e. very stable ylides. Nonetheless, it is a valuable alternative to the acylation of a simple ylide.

In 1968 Lloyd and co-workers[45] reported a new method for the preparation of stabilized arsonium cyclopentadienylides by condensing triphenylarsine oxide with cyclopentadienes, with or without electron-withdrawing groups, in the presence of either acetic anhydride or triethylamine-phosphorus pentoxide as the catalyst. For example, 1,2-dibenzoylcyclopentadiene (46) condensed with triphenylarsine oxide in acetic anhydride

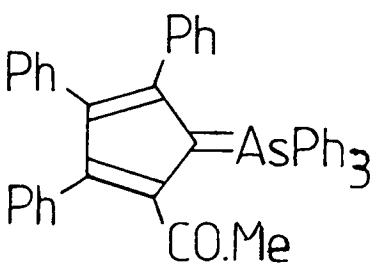
to give ylide (47), condensation taking place at the 4-position of the cyclopentadiene ring (Scheme Ten)[45].



(46) (47)

Scheme Ten

In another instance, 1,2,3-triphenylcyclopentadiene and triphenylarsine oxide gave two products, depending on the medium; (28) was obtained with triethylamine-phosphorus pentoxide, whereas (48) resulted from acetic anhydride as the condensing agent[45]. The latter ylide was presumably formed by the acetylation of the former ylide (28).

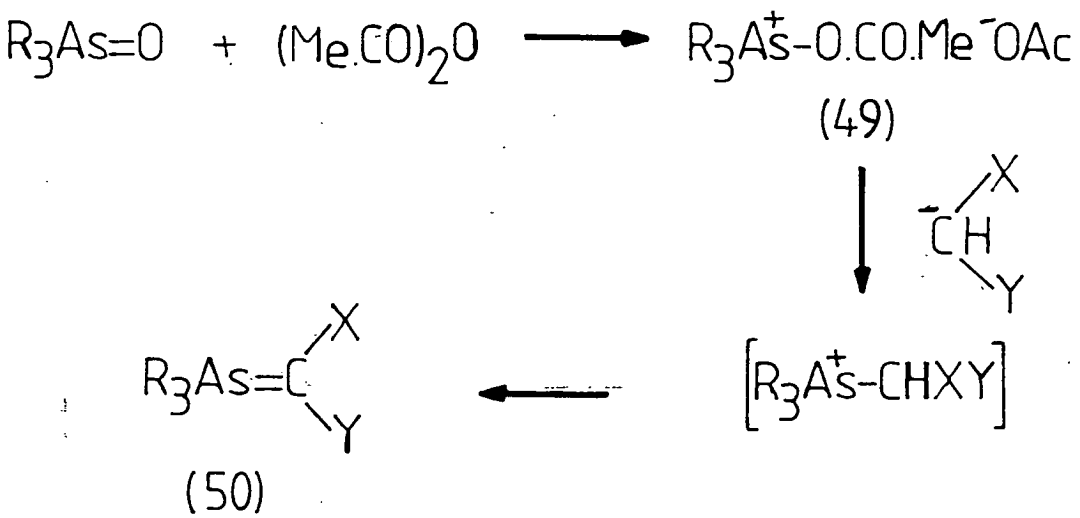


(48)

This method had previously been used for the preparation of sulphonium ylides from the reaction of sulphoxides with cyclopentadienes having electron-withdrawing substituents[46].

The generality of this reaction has been investigated by Gosney and Lloyd[40] who condensed

triphenylarsine oxide and tri-n-butylarsine oxide with a series of active methylene compounds in the presence of either acetic anhydride or triethylamine-phosphorus pentoxide to form arsonium ylides. The mechanism of these condensations points to the intermediate formation of an alkoxyarsonium salt (49) which undergoes nucleophilic attack by the enolate anion of the active methylene compound followed by proton loss to give the ylide (50) (Scheme Eleven).



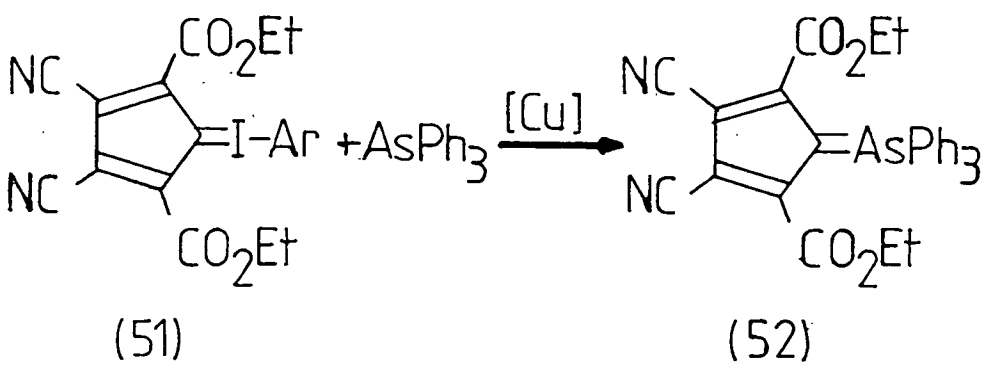
Scheme Eleven

To date the scope of this synthesis has been restricted to the more reactive methylene derivatives since considerable activation of the methylene group is necessary for ylide formation and less acidic compounds, e.g. fluorene, are completely inert.

1.2.4 Transylidation

Transylidation usually refers to the conversion of an ylide into another ylide by reaction with a

suitable substrate, e.g. with acetylenes[30], sulphines[30], N-acylaziridines[47] and acid chlorides[48]. These reactions will be discussed later in the section on reactions of arsonium ylides, but it is of interest to note that Friedrich and co-workers[49] have successfully prepared (52) by reacting aryliodonio-cyclopentadienes (51) with triphenylarsine (Scheme Twelve). Sulphonium, selenonium and phosphonium ylides have also been prepared by this route which is subject to catalysis by copper salts[49].



(51) (52)

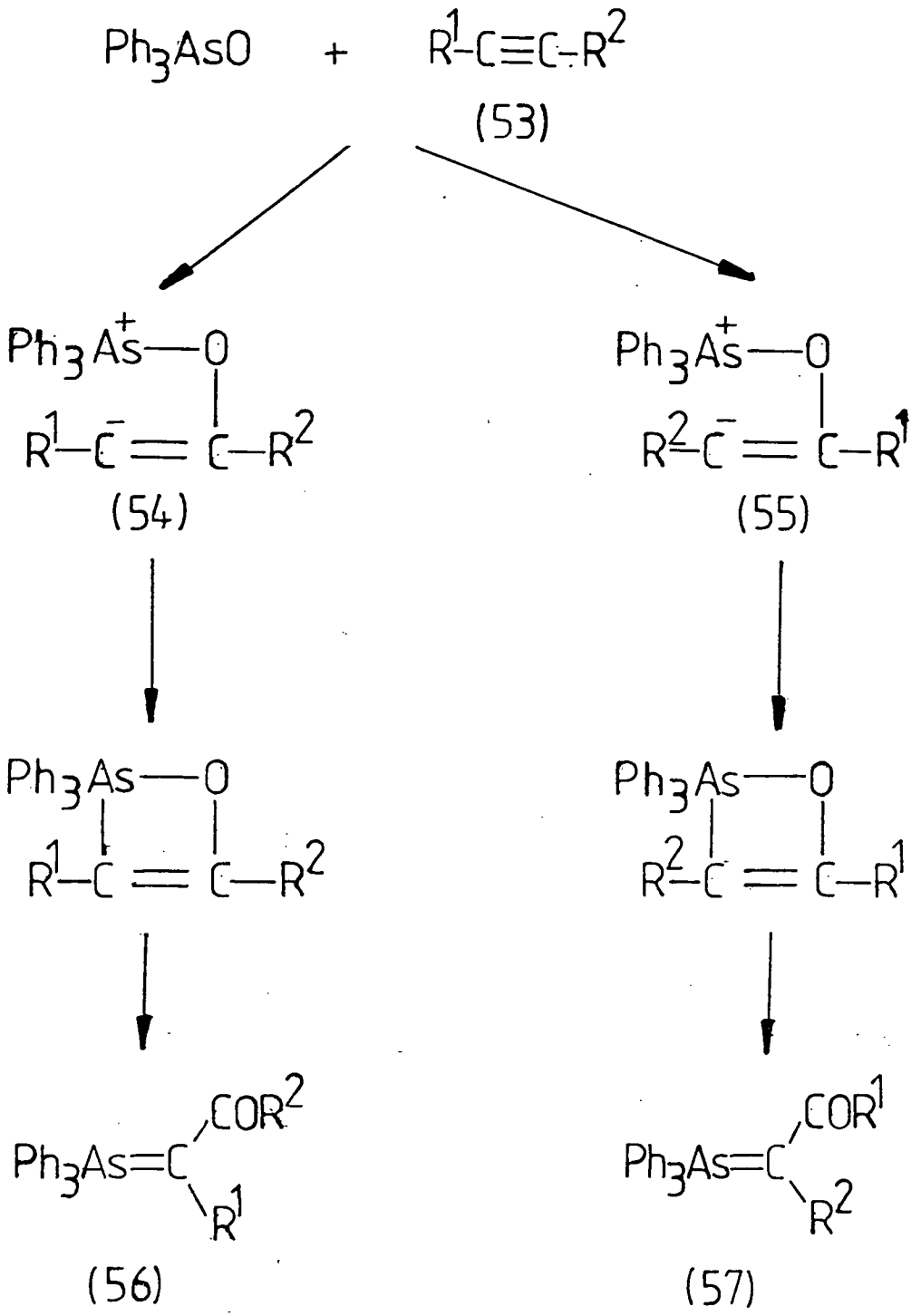
Ar = Ph, 4-MeC_6H_4, 4-$NO_2C_6H_4$

Scheme Twelve

In another study Schmidbaur and Tronich[28] observed that a 1:1 mixture of trimethylarsonium methylide and trimethylphosphine reacted to give an equimolar mixture of trimethylarsine and trimethylphosphonium methylide.

1.2.5 Reverse Wittig reaction

In a study of the reverse Wittig reaction, Ciganek[50] has reported a novel synthesis of arsonium



a) $R^1 = CO_2Me$; $R^2 = H$

b) $R^1 = CO_2Et$; $R^2 = Ph$

c) $R^1 = R^2 = CO_2Me$

d) $R^1 = R^2 = CF_3$

e) $R^1 = R^2 = CN$

Scheme Thirteen

ylides by reaction of triphenylarsine oxide with highly electrophilic acetylenes (53). In principle, two isomeric arsonium ylides could be formed in reactions involving unsymmetrically substituted acetylenes, but, with methyl propiolate and ethyl phenylpropiolate, ylide (56) was formed to the virtual exclusion of the ylide (57) (Scheme Thirteen). Apparently, the ester group of zwitterion (54) provides for better stabilisation of the negative charge than does hydrogen or phenyl in the alternative intermediate (55). As a result (56) is the observed product.

1.3 Properties of arsonium ylides

A review by Lloyd[51] touches briefly on the properties of arsonium ylides, some of which are also covered annually in the Journal of Organometallic Chemistry Cumulative Reports.

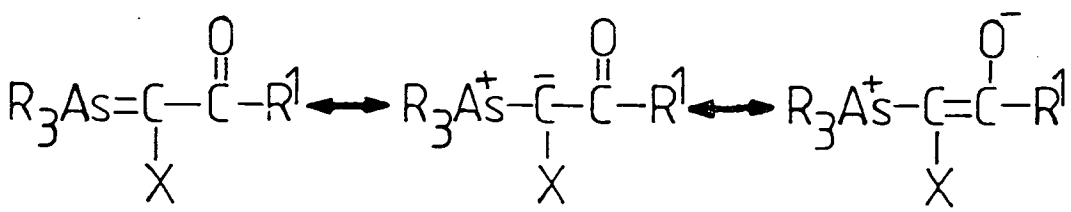
Compared with phosphonium and sulphonium ylides, the properties of arsonium ylides have received scant attention. By far the most widely investigated type of arsonium ylide are the acyl-substituted ylides, presumably because of their inherent stability. In general they are crystalline compounds with high melting points and can be stored at room temperature exposed to the atmosphere and moisture for at least several days without decomposition. The stability of ylides is often referred to and in general applies to the hydrolytic stability of the substances. There is no evidence to show any inherent thermodynamic instability associated with arsonium ylides as found with sulphonium

ylides (see Section 1.3.6).

The chemical instability associated with some arsonium ylides appears to be due to their reactivity towards water causing spontaneous hydrolysis in the atmosphere. As will be discussed later, the so-called 'unstable ylides' undergo an initial protonation in water followed by decomposition to afford an arsine oxide and a hydrocarbon. The 'stable ylides' are generally those ylides which can be handled in the atmosphere and do not react with water because of their low basicity and inability to undergo protonation.

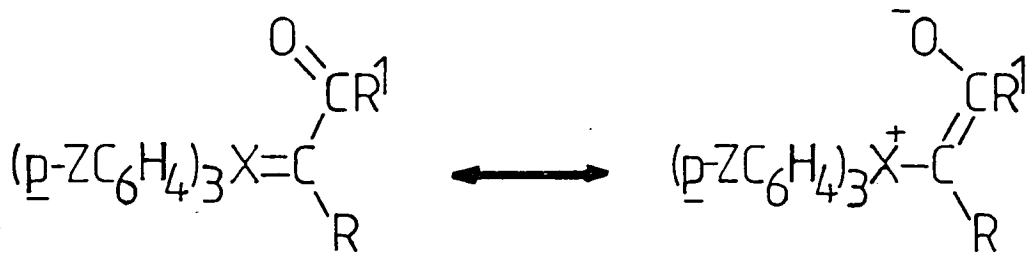
1.3.1 Infrared spectroscopy

An examination of the infrared spectra of acyl ylides and their conjugate acids provides some evidence regarding the role carbanion substituents play in stabilising arsonium ylides. The greater stability of these acyl ylides is undoubtedly due to the delocalisation of negative charge which is possible in the 'dipolar' canonical form (58b). Any shift in the carbonyl stretching frequency ($\nu_{C=O}$) in the substituent from the normal C=O region must be due to contributions such as (58c) to the resonance hybrid for the ylide.



(58a) (58b) (58c)

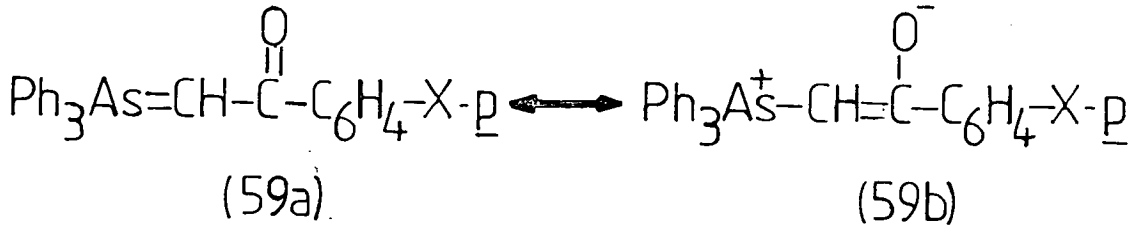
Table 1. Infrared data for ylides (60) X = As, P



(60a) (60b)

Z	R	R^1	$\nu_{C=O}^{KBr\ disc}$ (cm^{-1}) X = As	X = P
H	H	p-MeC_6H_4	1500	
H	H	p-PhC_6H_4	1506	
MeO	H	Ph	1506	
H	H	Ph	1514	1500
Me	H	Ph	1518	
H	H	Me	1525	1544
H	H	p-$NO_2C_6H_4$	1530	
H	H	NPh_2	1542	
H	Ph	OMe	1585	
H	H	OMe	1608	1621
H	CN	OMe	1640	

The stabilised ylides (59) show a carbonyl stretching frequency between 1505 and 1525 cm^{-1}, indicating a significant contribution to their structures from the resonance hybrid (59b) [52].

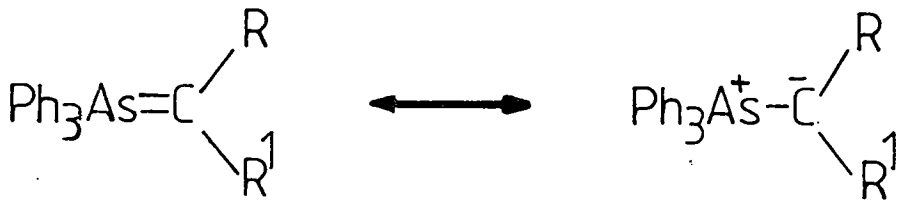


(59a) (59b)

Dale and Froyen[53] have reported the carbonyl stretching frequencies for a series of β-ketostabilised arsonium ylides (60) (Table 1). The tabulated values indicate that the contribution depends significantly on the nature of R^1 and parallels the ability of the attached group ($CO.R^1$) to stabilise a negative charge on the α-methylene carbon (CO_2Me < $CONPh_2$ < COMe < COPh). The additional delocalisation of the carbanionic charge by substitution of an electron-withdrawing group (R = CN) for R = H decreases the contribution of (60b) and raises the carbonyl stretching frequency.

The stable arsonium ylides (61, a-l) exhibit a similar lowering of the carbonyl stretching frequency by electron withdrawing groups (Table 2)[40]. The stretching frequencies associated with the ylides are uniformly low because of the delocalisation of the negative charge into these groups. The cyano stretching frequencies for ylides (61g) and (61k) are also low, occurring at 2170-2105 and 2145 cm^{-1}, respectively.

Table 2. Infrared data for ylides (61)



(61)

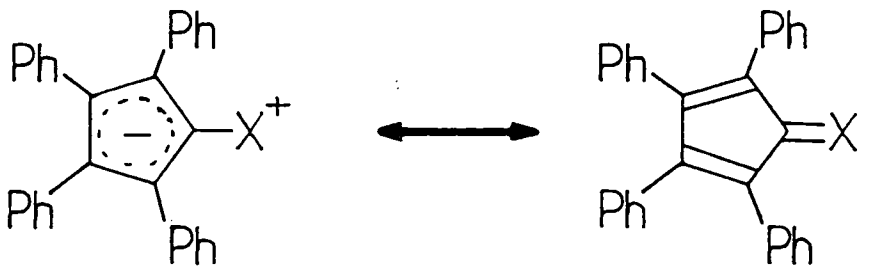
(61)	R	R^1	ν_{max}^{nujol} (cm^{-1})*
a	COPh	COPh	1581, 1568, 1505 (1520)[54]
b	COMe	COMe	1580, 1510 (1580, 1545)[54]
c	COMe	COPh	1578, 1555, 1515 (1560, 1530)[54]
d	COMe	COC_6H_4-NO_2-p	1565, 1515 (1570, 1530)[54]
e	SO_2Ph	SO_2Ph	1292, 1122 (1310, 1130)[55]
f	NO_2	COMe	1595, 1395
g	CN	CN	2170, 2140, 2105 (2200)[55]
h	CO_2Et	COPh	1640, 1523, 1500 (1675, 1530)[54]
i	CO_2Et	COMe	1645, 1535 (1640, 1540)[54]
j	COMe	CONHPh	1600, 1575, 1515
k	CN	CO_2Et	2145, 1625 (2200, 1640)[55]
l	CO_2Et	CO_2Et	1670, 1595 (1700, 1630)[55]

* N.B. Only maxima in the carbonyl, sulphonyl, nitro and nitrile regions are reported. Values for corresponding phosphorus ylides in brackets.

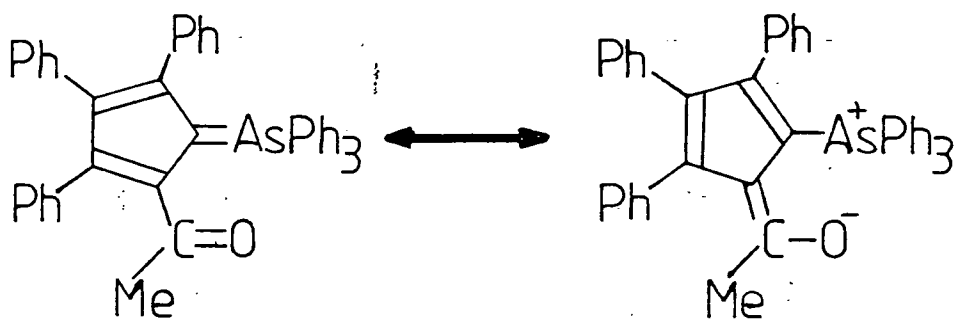
The stretching frequencies observed in arsonium ylides are significantly lower than those associated with the corresponding phosphonium ylides. This is in keeping with the assumption that the dipolar canonical forms make a greater contribution to the overall structure of arsonium ylides than they do in the case of phosphonium ylides. It follows that an examination of infrared data should permit a rough estimation of the relative reactivity of resonance-stabilised ylides of the type (61), since both the carbonyl stretching frequency and reactivity are clearly related to charge delocalisation. Accumulated chemical evidence in support of this supposition will be presented in section 1.4.

1.3.2 Dipole moment measurements

In view of the unique charge distribution that must exist in arsonium ylides, a study of their dipole moments must be expected to contribute to an understanding of their electronic structures. Of the few reports that have appeared, the most significant is that of Lumbroso[56] who observed the dipole moments of diphenylsulphonium, triphenylphosphonium, triphenylarsonium and triphenylstibonium tetraphenylcyclopentadienylides (62) to be 6.69, 7.75, 8.32 and 2.2 D respectively. Significantly the dipole moment increases with an increasing contribution from the canonical form (62a), thus indicating a decrease in $d\pi$-$p\pi$ overlap in the order: S>P>As>Sb. In the same paper triphenylarsonium 2-acetyl-3,4,5-triphenylcyclopentadienylide (48) was shown to possess an As,O-*cis* configuration (48b) in benzene, with a dipole moment of 5.29D.

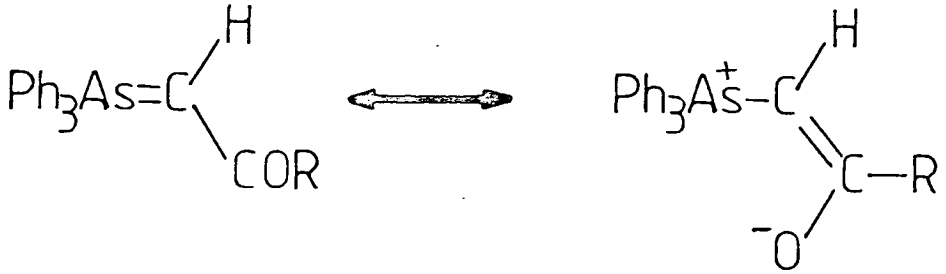


(62a) (62b)



(48a) (48b)

In another study Lumbroso[57] examined the dipole moments of triphenylarsonium acylmethylides (63) in benzene (Table 3) and elucidated their conformations. The acylmethylides were found to possess an As-O-cis conformation (63b)



(63a) (63b)

Table 3: Dipole moment data for ylides (63)

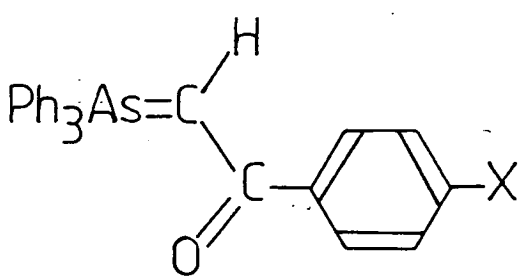
R	μ/D
Me	5.75
Ph	5.40
p-MeC_6H_4	5.37
p-$NO_2C_6H_4$	9.33

Johnson has also compared the dipole moment of triphenylarsonium fluorenylide (7.80D) with its phosphonium analogue (7.09D)[56,58] but, as was pointed out, it is difficult to evaluate the significance of the result in terms of multiple bonding since the required bond distance and bond angle information was unavailable.

From the meagre information, available, it is apparent that more data on bond lengths, bond angles, and electron density about the arsonium ylide bond are sorely needed before any accurate description of the electronic distribution in the ylide can be produced from dipole moment measurements.

1.3.3 Acidity and basicity measurements

A study of the basicity of arsonium ylides and/or of the acidity of their precursor salts has also shed some light on the electronic interactions taking place between the various structural components of the ylides. However, this aspect of arsonium ylide chemistry has been virtually neglected and only two comparative studies on the effects of carbanion substituents on the pK_a of arsonium salts have appeared to date. In the first, Nesmeyanov and co-workers[52] showed that the basicity of the ylide decreased consistently in a series of triphenylarsonium phenacylides (64) as the substituent X was made more electronegative (see Table 4).



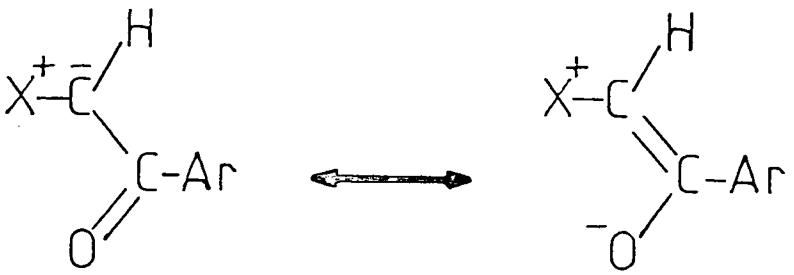
(64)

Table 4: pK_a values for salts of ylides (64)

Substituent X	OMe	Me	H	Cl	Br	NO_2
pK_a salt	9.16	8.97	8.52	8.02	7.95	6.67

Analogous trends have also been observed by Kabachnik[59] and Hudson[60] for a similar series of triphenylphosphonium phenacylides, and by Ratts and Yao[61] for a

series of dimethylsulphonium phenacylides. In each case the decrease in basicity was attributed to the increased delocalisation of the electron density of the carbanion through the adjacent phenacyl group, e.g. (65a) ↔ (65b).



(65a) (65b)

Nesmeyanov[52] found that the arsonium ylides (59) were 200-230 times more basic than the corresponding phosphonium compounds, from which he concluded that arsenic plays a smaller part than does phosphorus in the distribution of the negative charge. This can be accounted for in terms of the lower electronegativity of arsenic and perhaps to a greater diffusion of the 4d-orbitals, which prevents their effective overlapping with the 2p-orbitals at carbon.

In the other report, Froyen[21] established the order of basicity of a series of carbonyl-stabilised ylides (60). The ylides decreased in basicity in the expected order of decreasing carbanion-stabilising power of the attached group COR^1 : $CO_2Me > CONPh_2 > COMe > COPh$.

Froyen[21] also found a similar correlation for the reactivity of the ylides with p-nitrobenzaldehyde. The rate data showed the more reactive ylides to be the

more basic and vice-versa. Hudson and co-workers[60] have reported the same reactivity sequence for the corresponding phosphonium ylides. Such trends are to be expected since the electron density on the carbanion of an ylide ought to be reflected in its nucleophilicity to carbonyl compounds.

The nature of the substituents on the arsenic atom can also affect the basicity of arsonium ylides. Aksnes and Songstad[62] have determined the pK_a's of a variety of phenacylarsonium salts with different arsenic substituents and found that the replacement of methyl by phenyl leads to an increase in the acidity of the arsonium salts. Significantly this effect occurred irrespective of whether the heteroatom was arsenic, phosphorus or sulphur. In a later publication, Johnson and Amel[63] attributed the increase in acidity to the powerful electron-withdrawing effect of the phenyl groups (relative to alkyl) which decreases the electron density on the heteroatom. This lowering of electron density results in more double bond character in the carbon-heteroatom bond leading to a decrease in basicity and a better stabilisation of the ylide.

In recent years there has been much interest in the relative effectiveness with which different heteronium groups provide stabilisation for the adjacent carbanion. From the evidence available it is clear that stabilisation is afforded the carbanion by delocalisation of the negative charge through the carbon portion of the ylide, but the fact that such ylides have a finite existence points to additional stabilisation of the carbanion by the heteronium

group. The qualitative observation that the generation of ylides from arsonium salts requires stronger bases than are necessary for the conversion of both sulphonium and phosphonium salts to ylides can be correlated with the greater acidity of the sulphonium and phosphonium salts, and with the lower reactivity of the ylides derived therefrom, compared to their arsenic analogues.

Johnson and LaCount[64] have reported that the acidity of triphenyl-9-fluorenylphosphonium bromide (pK_a 7.5) in aqueous dioxan is about twice that of the analogous arsonium salt (pK_a 7.8). In the phenacylide series, the acidifying effect has been shown by Aksnes and Songstad[62], and later by Johnson and Amel[63] to decrease in the order: S>P>As, provided the heteroatom substituents are identical, i.e. all methyl or all phenyl, etc. These results agree with those of Lloyd and Singer[65] who found the effectiveness of different heteronium groups on the acidity of a number of heteronium salts of a series of tetraphenylcyclopentadienylides to be in the order: S>P>As>Sb.

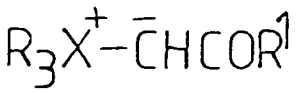
The observations that arsonium ylides are essentially more basic than the corresponding sulphonium and phosphonium compounds imply that arsenic plays a smaller part than sulphur and phosphorus in the distribution of the negative charge on the adjacent carbanion. This lower stabilisation provided by the heteroatom in arsonium ylides has been attributed by Johnson[58], amongst others[52,63,65], to the lower electronegativity of the arsenic atom and, in part, to the lowered effectiveness of

$p\pi$-$d\pi$ orbital overlap between the sp^2 carbon atom and the adjacent arsenic atom due to the greater diffusion of the arsenic 4d-orbitals. However, Isslieb and Lindner[66] have pointed out that factors other than the electronegativity of the heteroatom and the extent of d-orbital participation must play a part in determining the relative acidity of heteronium salts and, consequently, the stability of the derived ylides. They confirmed the fact that phosphonium salts are stronger acids than the corresponding arsonium compounds by comparing the acid dissociation constants in aqueous acetone of a number of compounds of the type $(Et_3MCH_2R)X$ where M was P, As or Sb, and R was $MeCO_2$ or PhCO. However the one stibonium compound studied ($R = CO_2Me$, $X = BPh_4$) was a considerably stronger acid (pK_a 8.5) than either the corresponding phosphonium (pK_a 10.6) or arsonium compound (pK_a 10.9). This relatively greater acidity of the stibonium salt was considered an anomaly and it was attributed to preferential solvation of the stibonium ylide.

1.3.4 N.m.r. spectroscopy

Proton n.m.r. spectroscopic studies have provided additional information about the geometry and electronic interactions in arsonium ylides. Whilst little attention has been focused on the question of π-interactions in the ylide bond, the significant shielding of the methine protons in arsonium ylides appears to mitigate against any extensive transfer of electron density from the carbanion to arsenic[21]. It has been pointed out that in systems As-Pd, there was no notable contraction

Table 5: Chemical shifts of methine protons of ylides (66)



(66)

R	R^1	Shift of methine proton (δ p.p.m.) X=As	X=P
Ph	OMe	3.15	
Ph	NPh_2	3.11	
p-$MeOC_6H_4$	Ph	4.08	
p-Me	Ph	4.60	
Ph	Me	3.98	3.67
Ph	p-MeC_6H_4	4.68	
Ph	p-PhC_6H_4	4.78	
Ph	Ph	4.71	4.4
Ph	p-$NO_2C_6H_4$	4.83	4.5

attributable to double-bonding between Pd and As, i.e. no appreciable $d\pi$-$d\pi$ bonding[67]. From the work of Johnson[11], it is apparent that tetracovalent phosphorus undergoes octet expansion (d-orbital resonance) to a greater degree than does similarly substituted arsenic. Nesmeyanov[52] has commented that this difference between P- and As-ylides is due to the greater diffusion of As 4d-orbitals, which permits their effective overlapping with the 2p-orbitals of carbon. Hence, n.m.r. arguments concerning chemical shifts will remain unaffected by $d\pi$-$p\pi$ bonding interactions.

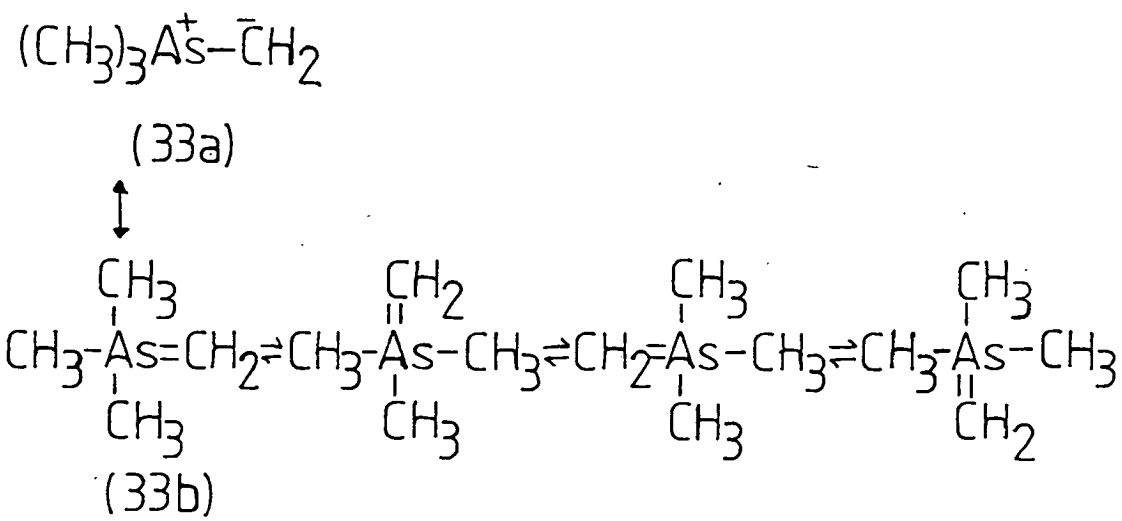
Chemical shift data for the methine proton in carbonyl-stabilised arsonium and phosphonium ylides (66) are recorded in Table 5[21,68]. Comparison of the shifts shows that X = P produces the greatest shielding at the methine proton, i.e. $\delta_{\text{As-methine}} > \delta_{\text{P-methine}}$, a surprising result in view of the significant lower basicity of the phosphorus compounds[58]. Another factor to be taken into consideration is the downfield shift of resonances due to deshielding by β-aryl rings. This can not be ignored and may possibly contribute to this anomalous difference in chemical shift.

Froyen[21] has shown that there is a fair correlation between the chemical shift of the methine proton of the arsonium ylides (66, X = As, R = Ph) and their reactivity towards p-nitrobenzaldehyde:

$$R = OMe > NPh_2 > Me > \underline{p}\text{-}MeC_6H_4 > Ph > \underline{p}\text{-}NO_2C_6H_4$$

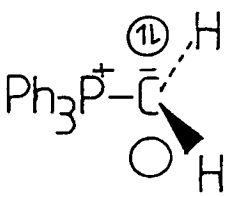
Such a trend is to be expected since the higher electron density on the carbanion of the more reactive ylides ought to be reflected in the chemical shift of the methine proton.

Schmidbaur and Tronich[28] have recorded the proton n.m.r. spectrum for trimethylarsonium methylide (33). The spectrum of a benzene solution at room temperature showed the expected singlet resonances at $\delta(CH_3)$ = -0.82 and $\delta(CH_2)$ = 0.19 p.p.m. The high field resonance for the methylene group indicated a considerable contribution from the resonance form (33a) to the actual structure of the ylide. At elevated temperature the CH_2 as well as the CH_3 signals displayed line broadening which was reversible on cooling, but coalescence could not be observed owing to the facile decomposition of (33) above 60°C. The observed line broadening is consistent with the view that above room temperature the carbanionic function is not localised at only one site but is subject to a fast proton exchange process involving the three methyl groups. Interestingly, coalescence of the resonances could readily be accomplished at room temperature by the addition of traces of a protic acid to catalyse rapid intermolecular proton exchange between the ylide molecules (Scheme Fourteen).

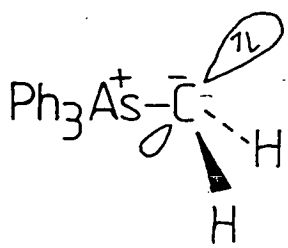


Scheme Fourteen

Yamamoto and Schmidbaur[26] have elucidated the structure of triphenylarsonium methylide (30) in solution using ^{13}C-n.m.r. spectroscopy. They found that $^{1}J_{CH}$ values for the methyltriphenylarsonium halides (Cl: 142.0; Br: 142.0; I: 142.0 Hz) showed a slight reduction upon conversion to the methylide (136.7 Hz) whereas the coupling constant was greatly increased in the corresponding phosphorus system[69]. In the latter case the change in coupling constant was thought to be a consequence of an effective $sp^3 \rightarrow sp^2$ rehybridisation of the carbon atom upon ylide formation giving rise to a planar structure (67). The result was in accord with a later X-ray analysis[26]. By comparison, the bonding of the ylidic carbon in (30) seems to be virtually unchanged (sp^3), indicating a pseudo-tetrahedral geometry, i.e. (30a).

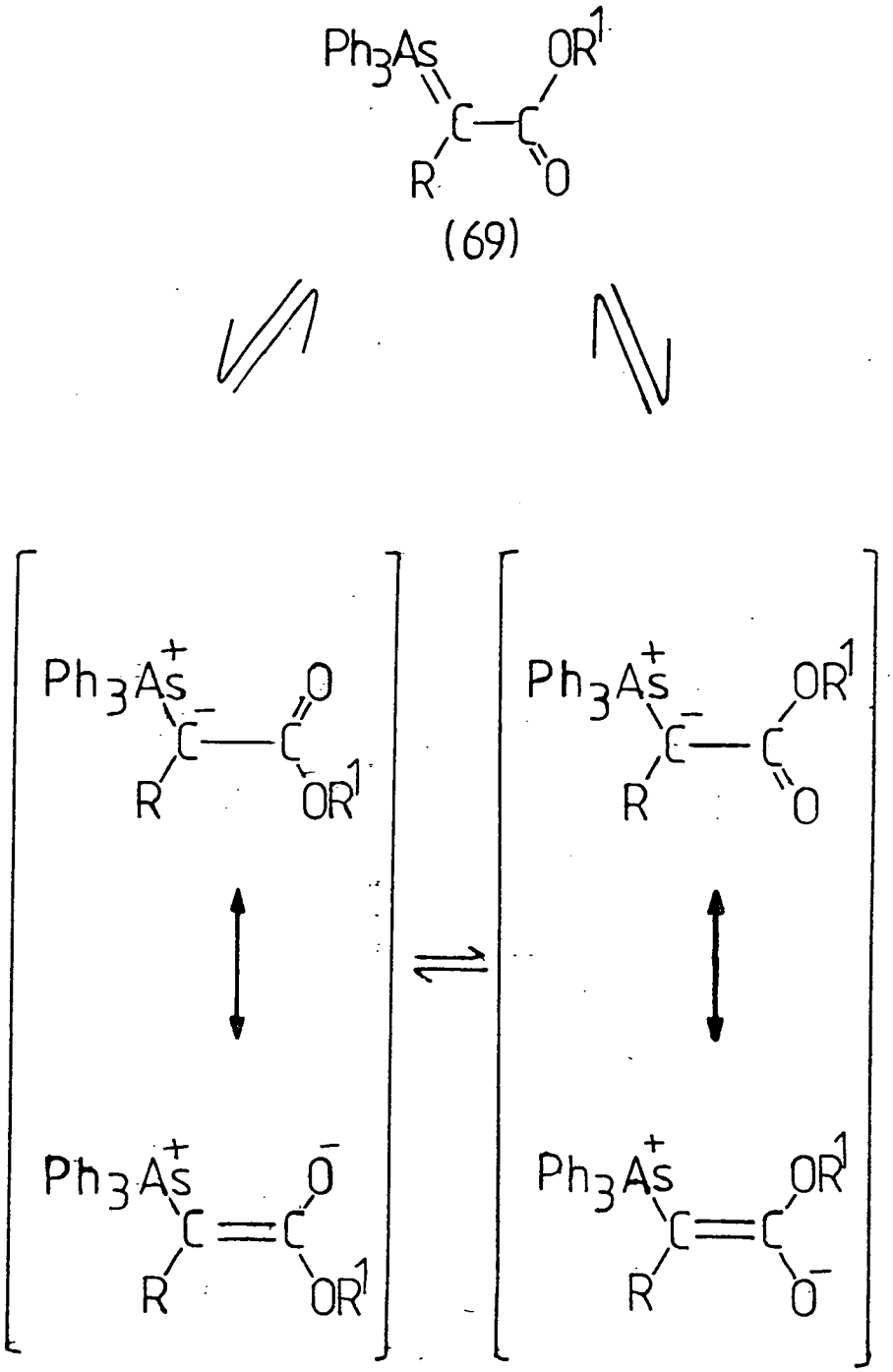


(67)



(30a)

In a report concerning the proton n.m.r. spectra of heteronium cyclopentadienylides (68a ↔ 68b), Ernstbrunner and Lloyd[70] have evaluated the chemical shifts and coupling constants of the protons attached to the five-membered ring, from which they calculated the bond



Scheme Fifteen

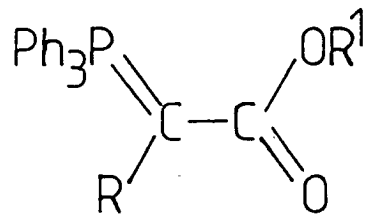
orders[71,72]. From these calculations, Ernstbrunner and Lloyd concluded that the arsonium ylide (68, X = $AsPh_3$) was more delocalised and had more cyclopentadienide character than the corresponding phosphonium (68, X = PPh_3) and sulphonium (68, X = SMe_2) ylides, in keeping with other comparative studies[38,59].

(68a) (68b)

Froyen and Dale[73] have studied the intramolecular dynamics of a number of α-carbonylstabilised arsonium ylides (69) using n.m.r. spectroscopy. They demonstrated the existence of a cis/trans equilibrium (Scheme Fifteen) by the observation at low temperature of two chemically different methoxy groups for (69; R^1 = Me; R = H, Ph, CN), coalescence of which could be brought about by raising the temperature. The rotamer ratio (K cis/trans) at coalescence showed a strongly preferred cis configuration, favoured presumably by the coulombic interaction between the oxyanion and arsonium group. Similar observations have been reported by Casanova and Rutolo[74] for the related sulphonium ylide, dimethylsulphonium carbomethoxymethylide.

Comparison of Froyen's results with the proton n.m.r. data obtained by Bestmann and co-workers[75] for the corresponding phenacylide (70; R^1 = Me; R = H, Ph) revealed

a lower rotamer ratio for the arsenic derivatives. To account for this difference, Froyen suggested that the phosphorus orbitals overlap with the oxygen 2p-orbitals more effectively than do the more diffuse arsenic orbitals, giving rise to a P---O interaction that is more bonding than the As---O interaction. It is then expected that stronger contraction of the arsenic orbitals should lead to stronger bonding, this conclusion being supported by the greater cis/trans rotamer ratio when R = CN (7.2) compared with R = H (2.0), Ph (2.3) for (69).

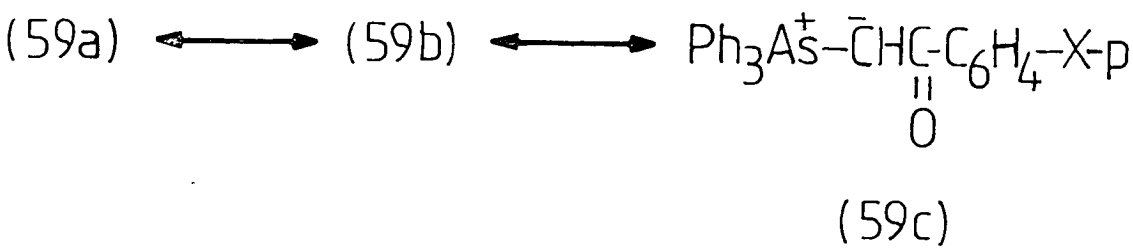


(70)

In a later study, Dale and Froyen[53] examined a series of β-ketostabilised arsonium ylides for evidence of similar cis/trans equilibria. They found no sign of any temperature dependence in the proton n.m.r. spectra of these compounds or related phosphonium and sulphonium ylides that could be attributed to restricted rotation about the enolate C-C bond. However, Johnson and Schubert[12] observed the broadening of the methine resonance in the proton n.m.r. spectrum of triphenylarsonium phenacylide (22), and concluded that this was the result of a protolytic

exchange reaction analogous to that reported for triphenylphosphonium phenacylide[76]. That keto derivatives should exist on the n.m.r. timescale as static conformers while ester stabilised ylides rotate readily can be rationalised by postulating a stronger coulombic interaction between the heteronium group and the oxyanion in β-ketoylides due to the greater polarity of the carbonyl bond[77]. It seems reasonable to assume that such an interaction would effectively counteract internal rotation especially in view of the relatively non-polar media employed[78].

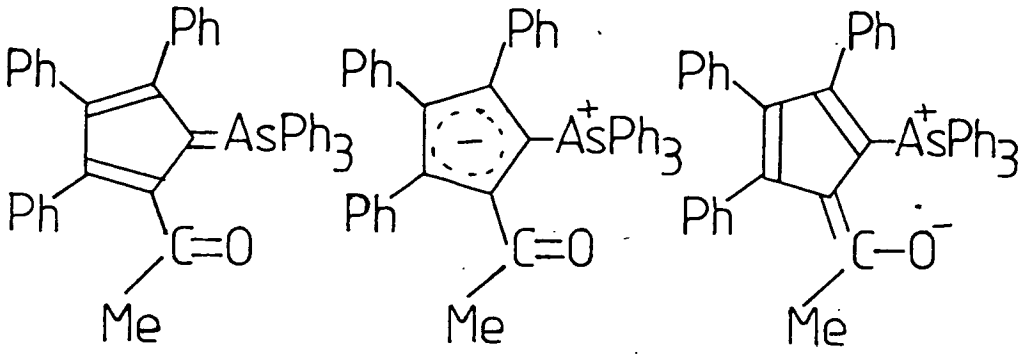
In the only detailed ^{13}C-n.m.r. spectroscopy study, Froyen and Morris[79] have investigated substituent effects for a series of stabilised arsonium ylides (59; X = H, Me, OMe, F, Cl, Br, CN, NO_2, Ph). They observed a linear dependence of the dual parameters of Swain and Lupton[80] with the chemical shifts of the ylide carbon, but a similar correlation was not obtained with the chemical shifts of the carbonyl carbon. The chemical shifts of the carbon atoms in the phenyl groups linked to arsenic indicated a limited interaction between aromatic ring carbons and arsenic. The ylide carbon, which may be regarded as sp^2 hybridised, is shielded by ca. 10 p.p.m. with respect to an olefinic, sp^2 hybridised carbon, reflecting the presence of high electron density on the ylide carbon as indicated by the canonical structure (59c).



(59c)

1.3.5 X-ray diffraction measurements

In 1971, Lloyd and co-workers[81] published the first crystallographic structure analysis for an arsonium ylide, namely triphenylarsonium 2-acetyl-3,4,5-triphenylcyclopentadienylide (48). The reported structural data gave support to previous speculation as to the nature of the electronic distribution in ylides in general[56,57]. Thus, the significant shortening of the C(1)-As bond length and C(1)-C(2) distance provided evidence for the delocalisation of the negative charge through the cyclopentadienylide system, probably via π-bonding and the participation of canonical forms (48a) and (48b). However, neither of these forms was consistent with the low value (1565 cm^{-1}) of the carbonyl stretching frequency in the i.r. spectrum. The molecular dimensions also established that a dipolar form (48c) with an $As^{+}---O^{-}$ intramolecular interaction made a considerable contribution to the ground state structure, thus explaining the I.R. spectrum. The authors accounted for the bond length distribution in and around the 5-membered ring by proposing population densities of the order: 30-35% for (48a), 20-30% for (48b) and 40-45% for (48c).

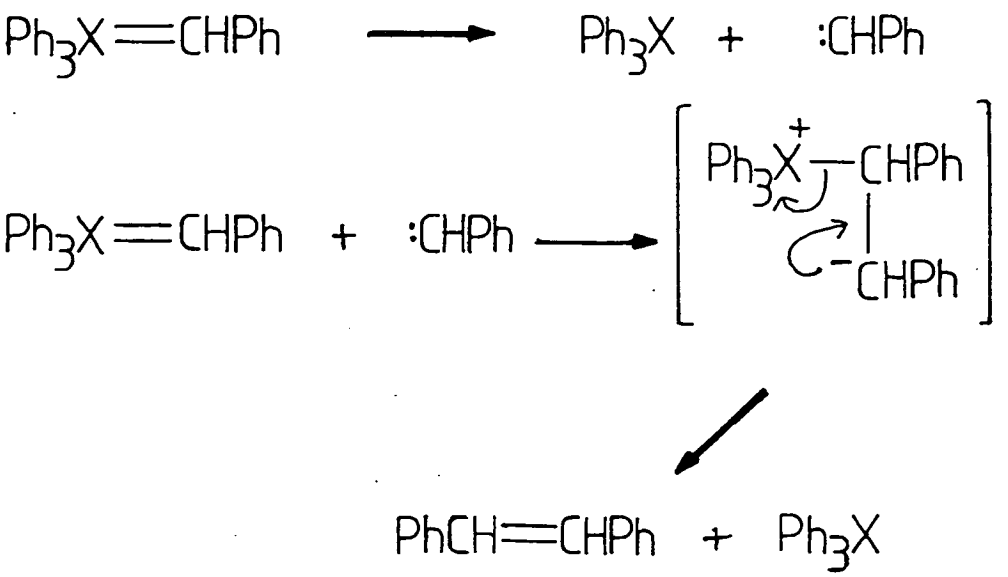


(48a) (48b) (48c)

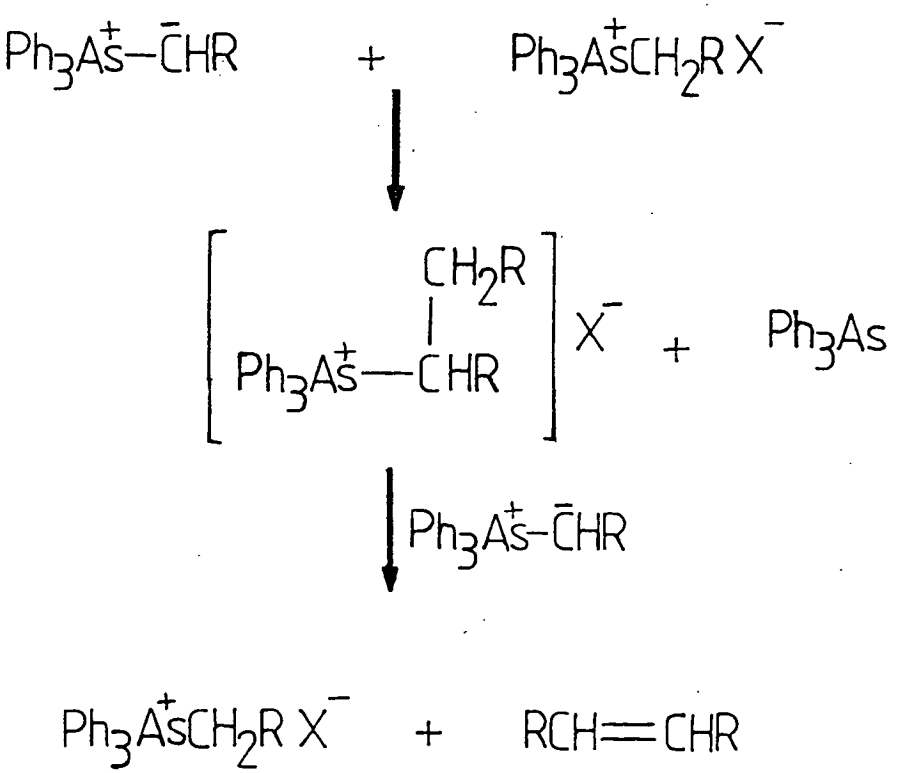
1.3.6 Thermal stability

There have been relatively few studies concerned with the thermal stability of arsonium ylides, presumably because thermal decomposition has not proved to be a problem as with sulphonium and, in some cases, phosphonium ylides. From the work reported to date it appears that arsonium ylides are essentially more stable than sulphonium ylides but less stable than their phosphonium analogues.

Thus, Nesmeyanov and co-workers[82] have reported that triphenylarsonium benzylide decomposed in boiling benzene-ether solution to give triphenylarsine (50-60%) and a mixture of stilbene isomers (70-80%). By contrast, triphenylphosphonium benzylide is stable under these conditions, although Trippett[83] has reported that the corresponding phosphonium salt, when fused with sodium methoxide (about 240°C) gives triphenylphosphine and stilbene as major products, apparently via a carbene



Scheme Sixteen



Scheme Seventeen

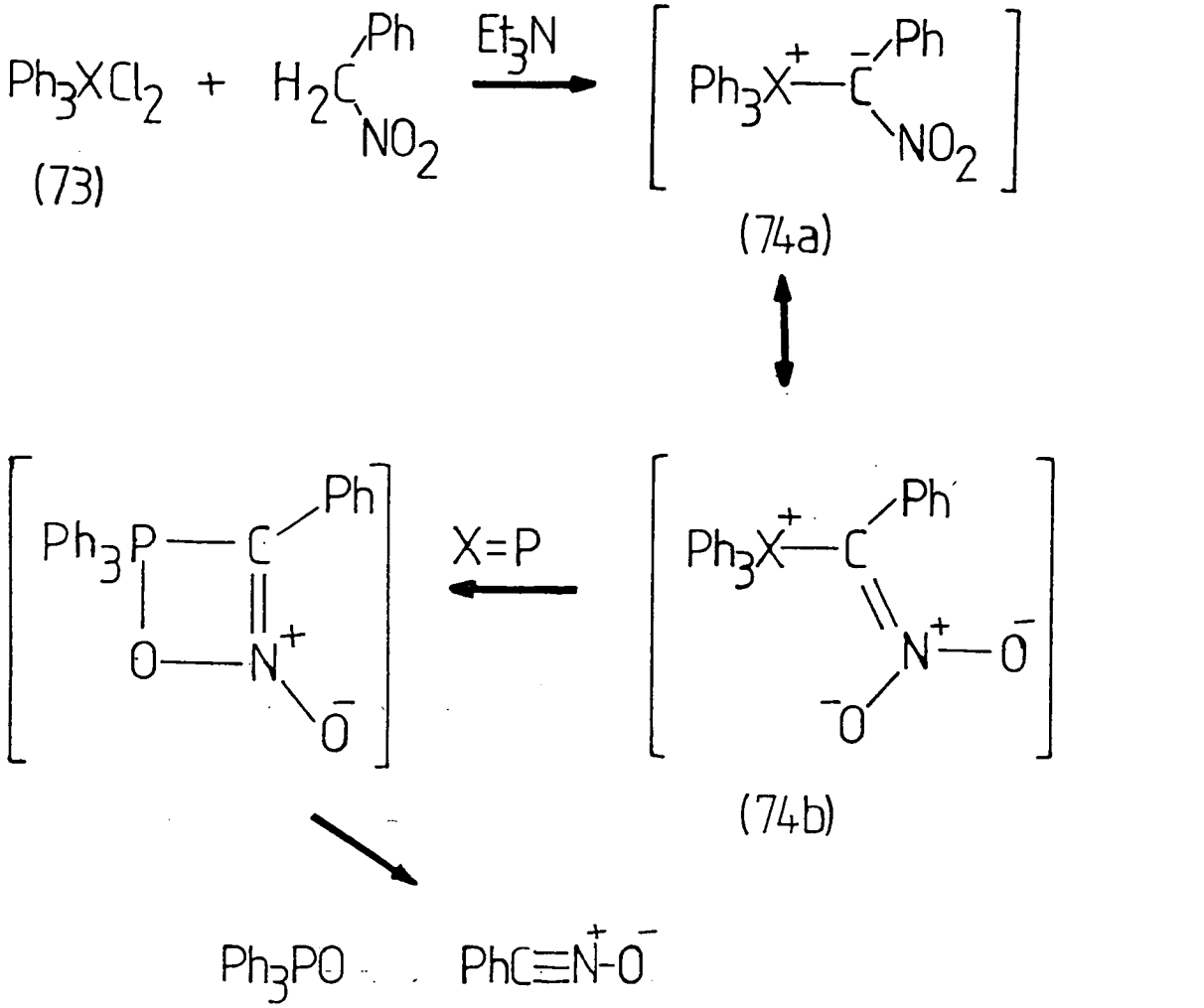
mechanism as shown in Scheme Sixteen. Similarly, the simplest arsonium ylide, namely trimethylarsonium methylide, decomposes to give trimethylarsine and ethene[28].

Nesmeyanov[82] proposed two distinct mechanisms to account for the decomposition of triphenylarsonium benzylide. The first mechanism involved the formation of a carbene or carbenoid intermediate *via* the unimolecular dissociation of the ylide and the subsequent trapping of this intermediate by the nucleophilic ylide to form a zwitterion, which eliminated triphenylarsine to give the olefin. This mechanism is shown in Scheme Sixteen.

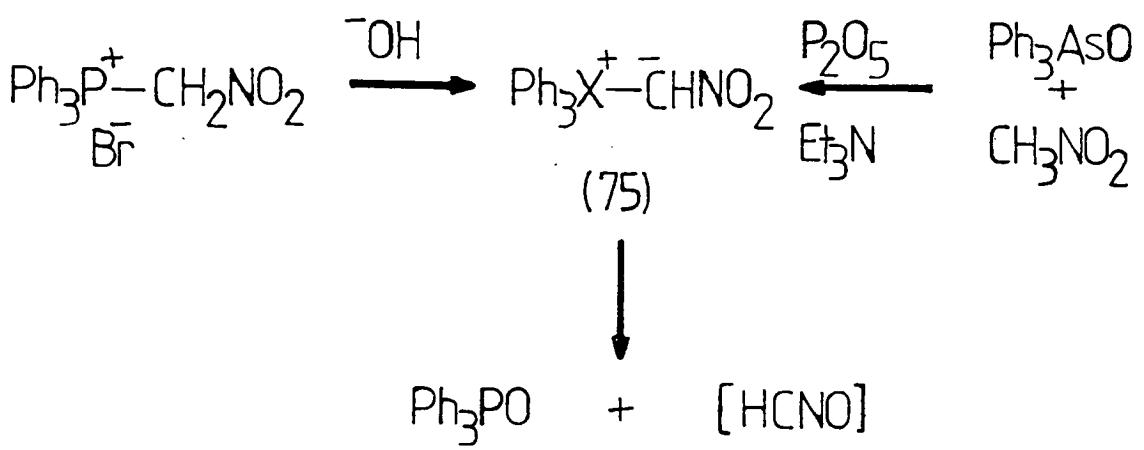
The second overall mechanism is outlined in Scheme Seventeen, and proceeded *via* an ionic chain reaction in which unreacted arsonium salt played the role of the catalyst. This mechanism, favoured by the authors, was supported by the detection of minute amounts of arsonium salt in the reaction mixture, even when only a small excess of phenyllithium was used. Furthermore, a large excess of base greatly retarded the reaction while a deficiency accelerated it.

The thermal stability of triphenylarsonium phenacylide (22) has been investigated by Johnson and Schubert[12]. The ylide could be recovered unchanged after prolonged heating in benzene but decomposed on boiling in toluene to give *trans*-1,2,3-tribenzoylcyclopropane (71) and triphenylarsine. The corresponding sulphonium ylide behaved similarly, but the phosphonium

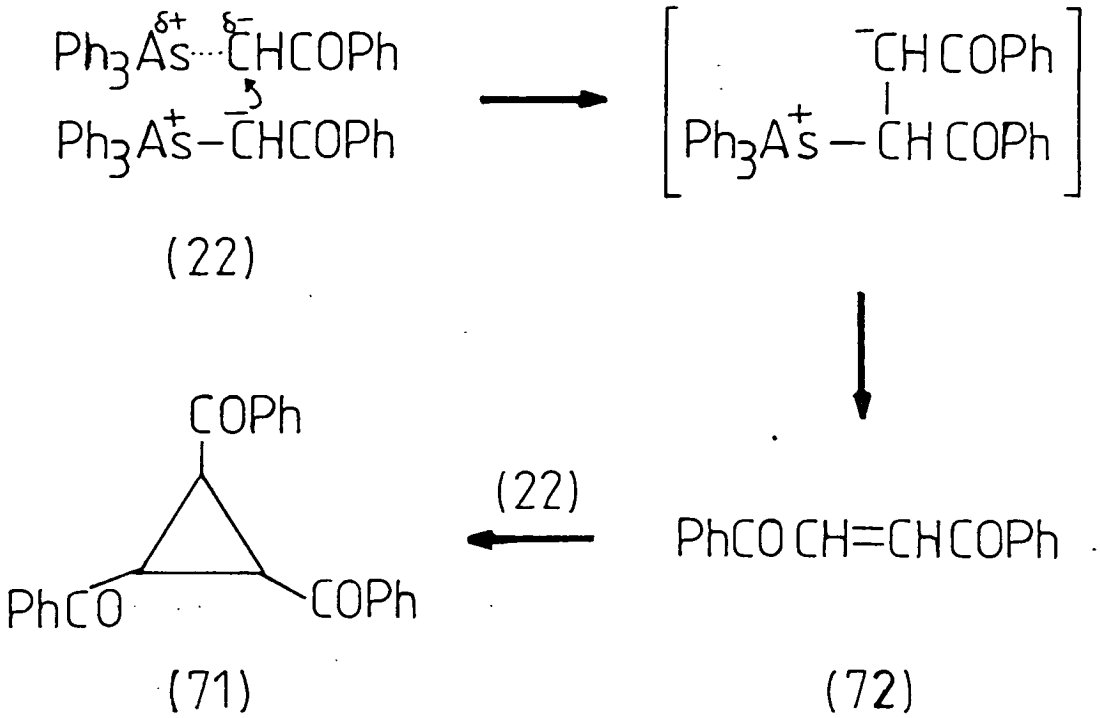
analogue proved to be stable under these conditions[84]. To account for the formation of (71), these authors proposed the mechanism shown in Scheme Eighteen, but no attempt was made to trap a carbene fragment, although an attempt to trap the olefin (72) with 2,5-diphenylisobenzofuran failed. The only evidence to support a carbene/carbenoid mechanism is the observation that it is a thermal reaction occurring in inert solvents, and by analogy with the thermal decomposition of sulphonium ylides in which carbenes have been trapped[85]. Alternatively, the olefin (72) may have been produced by an ionic chain reaction as shown in Scheme Seventeen. This mechanism is supported by the observation that reaction of the ylide with phenacyl bromide (or with the conjugate acid of the ylide) also afforded the cyclopropane. It was suggested that any proton source, moisture or traces of arsonium salt would serve as the chain-carrying agent. In both mechanisms, the final step involves the Michael addition of triphenylarsonium phenacylide to olefin (72). The authors have shown that this addition does occur with authentic olefin, thus supporting its intermediacy.



Scheme Nineteen



Scheme Twenty



Scheme Eighteen

The failure by Nesmeyanov[82] to obtain 1,2,3-triphenylcyclopropane from the decomposition of the non-isolable arsonium ylide, triphenylarsonium benzylide (15) may be due to the lack of an electrophilic centre in the resulting stilbene, thus rendering the olefin unsusceptible to Michael addition by unreacted ylide.

In a few cases arsonium ylides have proved to be more stable than their phosphorus analogues. For example, Horner and Oediger[44] failed to obtain the phosphonium ylide (74, X=P) from the reaction of triphenylphosphinedichloride (73, X=P) with phenylnitromethane in the presence of triethylamine. Instead they isolated triphenylphosphine oxide together with benzonitrile oxide, apparently by an intramolecular transfer of oxygen via a four membered transition state as shown in Scheme Nineteen. By contrast,

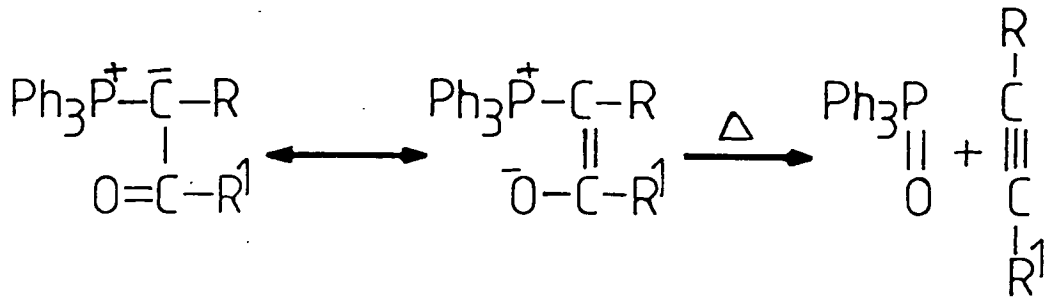
the analogous arsonium ylide could be prepared in reasonable yield from the corresponding reaction with triphenylarsine dichloride[44].

A similar rearrangement has been observed by Trippett and Walker[86] in an attempt to prepare triphenylphosphonium nitromethylide (75, X=P) from the reaction of nitromethyltriphenylphosphonium bromide with aqueous hydroxide (Scheme Twenty). They were able to isolate only triphenylphosphine oxide, but did detect the presence of the fulminate ion. In marked contrast to this observation, Gosney and Lloyd[40] have prepared the arsonium analogue (75, X=As) and found it to be stable under similar conditions. They did, however, observe such a rearrangement in the mass spectrometer.

This marked difference in stability between these phosphonium ylides and their arsonium analogues presumably results from the formation of a highly stable phosphorus-oxygen bond which acts as the driving force for the observed decompositions. On the other hand, triphenylarsine is not a particularly strong oxygen scavenger, and in this connection it is worth noting that Ciganek[50] has shown that triphenylarsine oxide readily transfers its oxygen to triphenylphosphine.

Unlike their arsonium analogues, keto-stabilised phosphonium ylides give rise to triphenylphosphine oxides and acetylenes[87,88,89] upon thermal decomposition (Scheme Twentyone). To date, no analogous reaction has been reported for arsonium ylides but the reverse reaction of triphenylarsine oxide with electrophilic acetylenes

does proceed readily to give arsonium ylides[50].



Scheme Twentyone

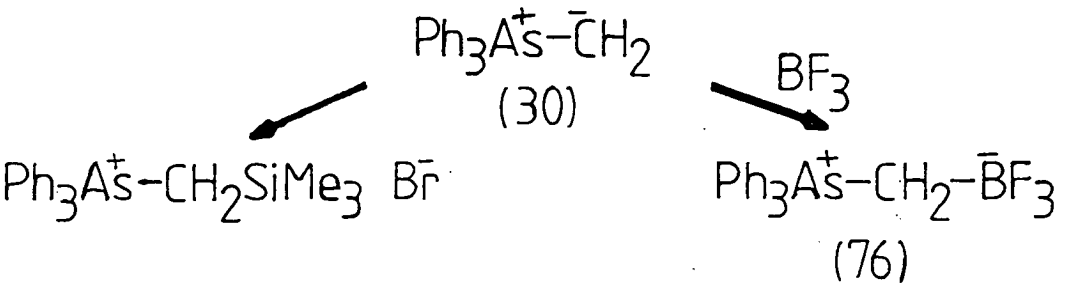
1.4 Reactions of arsonium ylides

There are basically two types of reactions which ylides undergo. The first type are those in which only the carbanion is involved mechanistically (carbanionic reactions). This group of reactions consists mainly of those reactions which any carbanion, regardless of structure, would undergo. The only effect of the heteroatom portion in these reactions is to moderate the nucleophilicity exhibited by the carbanion. The second, and by far the most interesting group of reactions of ylides are those in which both the carbanion and the heteroatom portion are involved. In this group falls the Wittig reaction which acted as a stimulus for much research into ylide chemistry. Such reactions rely on the ability of the heteroatom to become pentavalent in an intermediate or transition state of the reaction. Studies of the mechanisms of these reactions and the physical properties of ylides have aroused interest in the study of valence shell

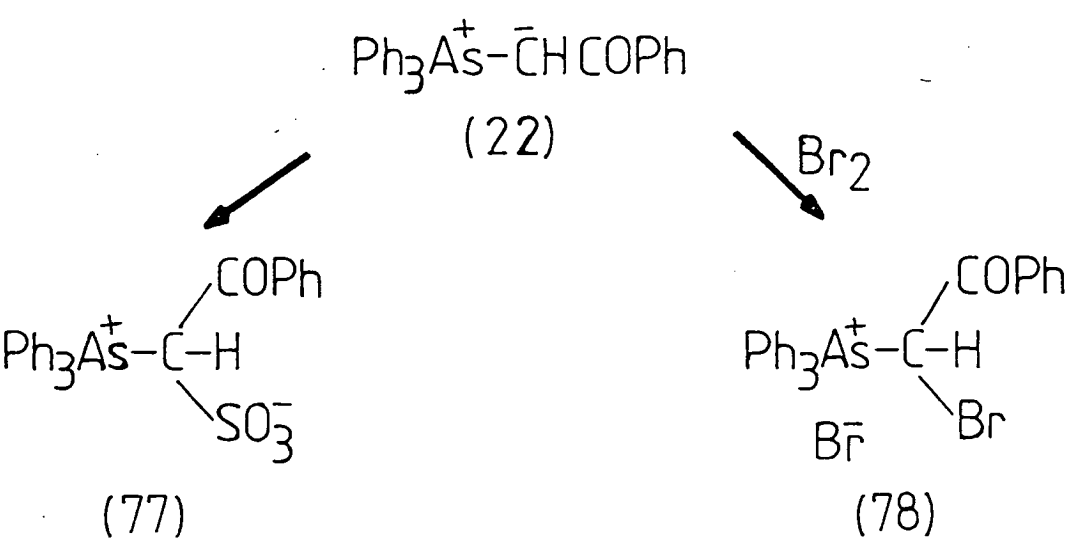
expansion by elements of the second and lower periods.

1.4.1 Carbanionic reactions

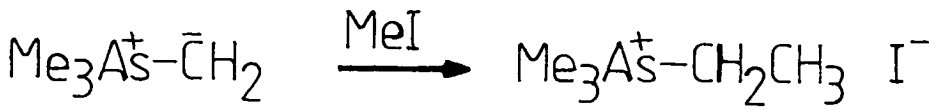
The nucleophilic nature of arsonium ylides was first verified in 1961 by Seyferth and Cohen[25] who demonstrated that triphenylarsonium methylide (30) could be alkylated with trimethylsilyl bromide in a typical displacement reaction. In the same publication, triphenylarsonium methylide was reported to react with boron trifluoride to give a 1:1 adduct (76).



In 1964, Nesmeyanov[18] reported the reaction of triphenylarsonium phenacylide (22) with sulphur trioxide and bromine to give a sulphobetaine (77) and an arsonium salt (78), respectively. In this way, arsonium ylides behave in a similar fashion to their phosphorus analogues[90].

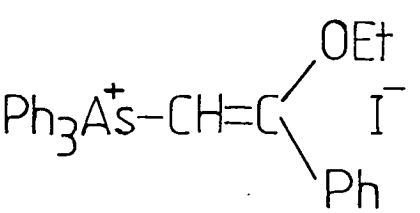


Several years later, Schmidbaur and Tronich[28] showed that trimethylarsonium methylide (33) resembled its phosphorus analogue[91] chemically in that it could be alkylated with methyl iodide to give almost quantitative yields of trimethylethylarsonium iodide (79).



(33) (79)

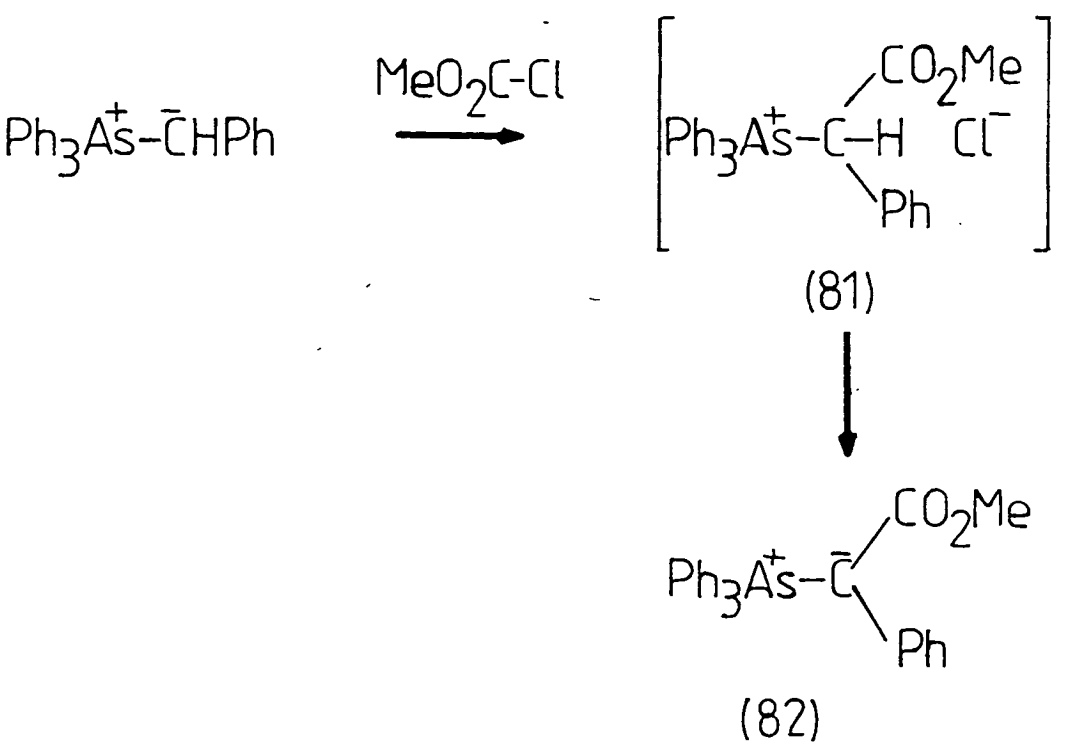
By comparison, Johnson and Schubert[12] found that the stabilised ylide triphenylarsonium phenacylide did not undergo normal alkylation on treatment with ethyl iodide, but instead afforded the O-ethyl product (80). This result is identical with the O-alkylation reported for the phosphonium analogue[92] but contrasts with the C-alkylation observed for the corresponding sulphonium ylide[84]. Furthermore, this result contrasts with the apparent C-alkylation of triphenylarsonium phenacylide by phenacyl bromide observed by the same authors.



(80)

In a related study[93] the use of the very reactive reagent trimethyloxonium tetrafluoroborate as alkylating agent led to O-alkylation of the sulphonium ylide. This may indicate that the reaction is under kinetic control and that C-alkylation results from thermodynamic control.

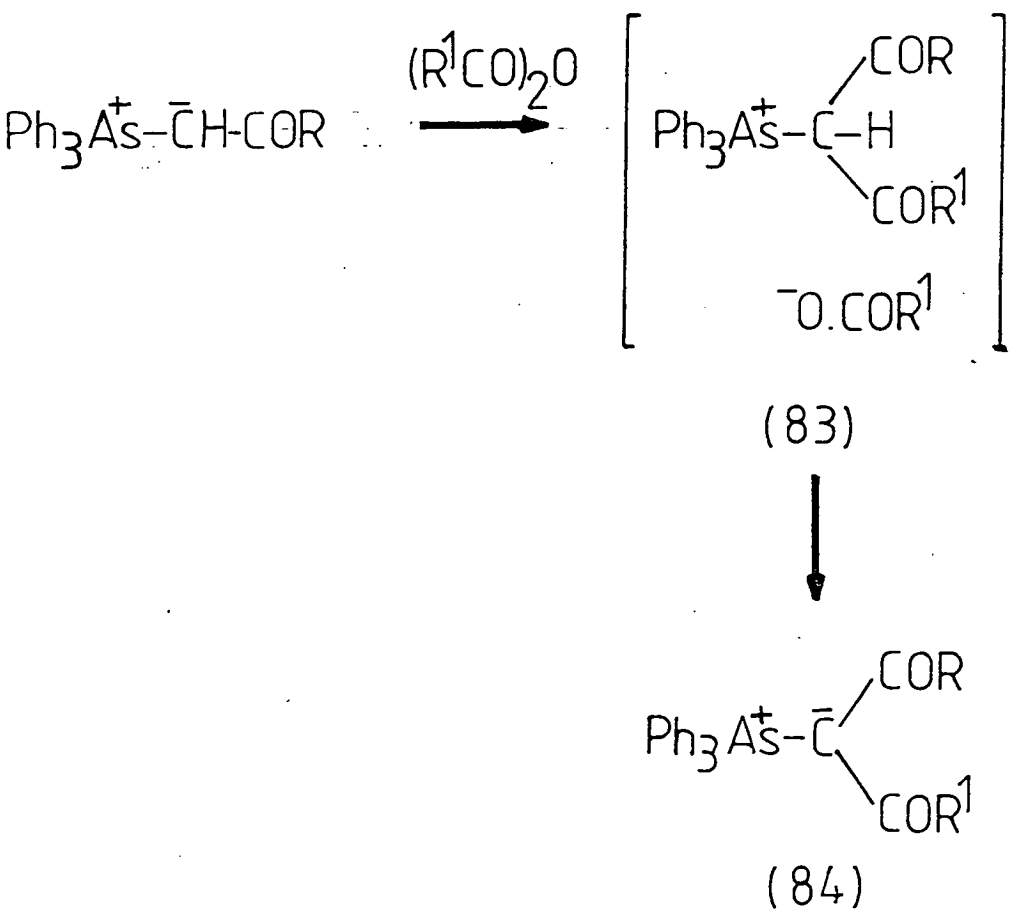
Acylation of phosphonium and sulphonium ylides has been used extensively as a method for the conversion of simple ylides into complex carbonyl substituted ylides. This transylidation reaction has been extended to arsonium ylides. For example, Dale and Froyen[73] have prepared triphenylarsonium α-carbomethoxybenzylide (82) by acylating triphenylarsonium benzylide with methyl chloroformate. This reaction presumably proceeds via the formation of the intermediate arsonium salt (81) followed by proton abstraction to give ylide (82) as shown in Scheme Twentytwo.



Scheme Twentytwo

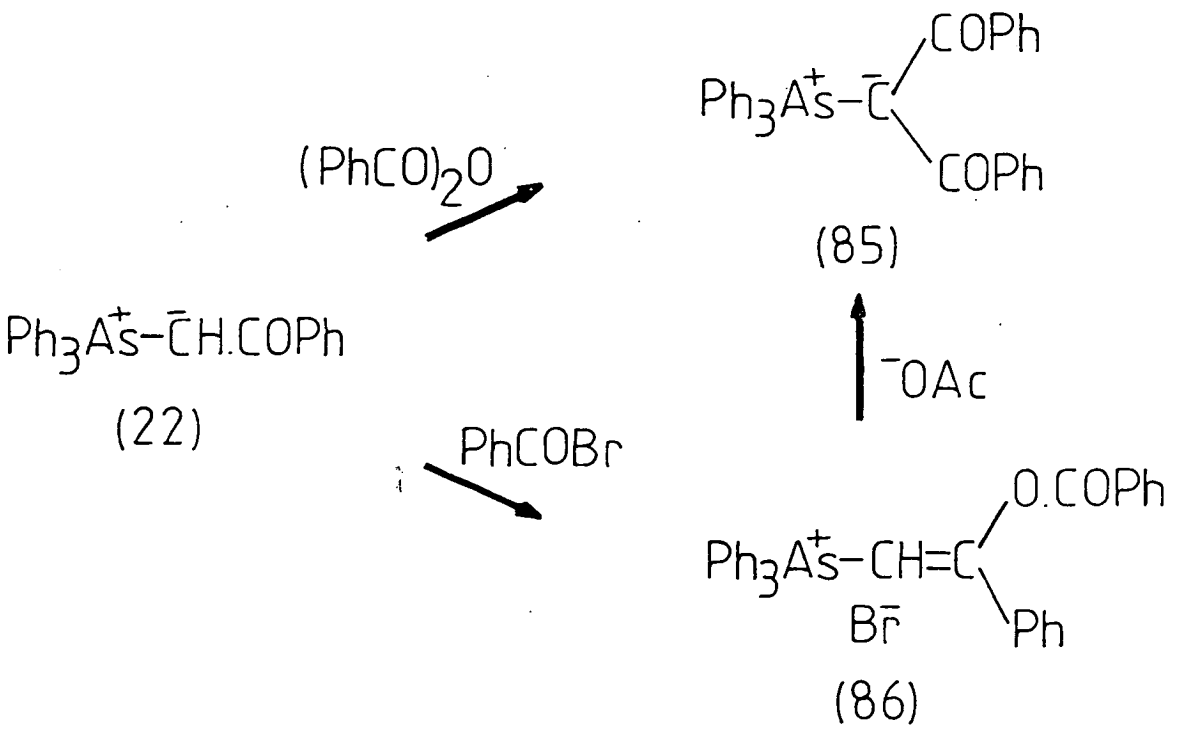
Johnson and Schubert[12] concurrently reported the acylation of triphenylarsonium methylide with benzoyl chloride, benzoic anhydride, or ethyl benzoate to give the more highly stabilised ylide, triphenylarsonium phenacylide.

Practically all other acylation studies have involved β-carbonyl ylides with the possibility of competing C- and O-acylation. Thus, Gosney and Lloyd[40] have acylated several ylides with acid anhydrides and found that C-acylation occurs with the formation of ylide (84) by direct loss of a proton from the very acidic intermediate salt (83) (Scheme Twentythree).



Scheme Twentythree

Johnson and Schubert[12] have shown that the course of this acylation varied with the nature of the acylating agent. Thus, treatment of triphenylarsonium phenacylide with benzoyl bromide gave the enol benzoate (86) which, on treatment with sodium acetate, gave triphenylarsonium dibenzoylmethylide (85). However, reaction of ylide (22) with benzoic anhydride led to direct C-acylation as shown in Scheme Twentyfour.



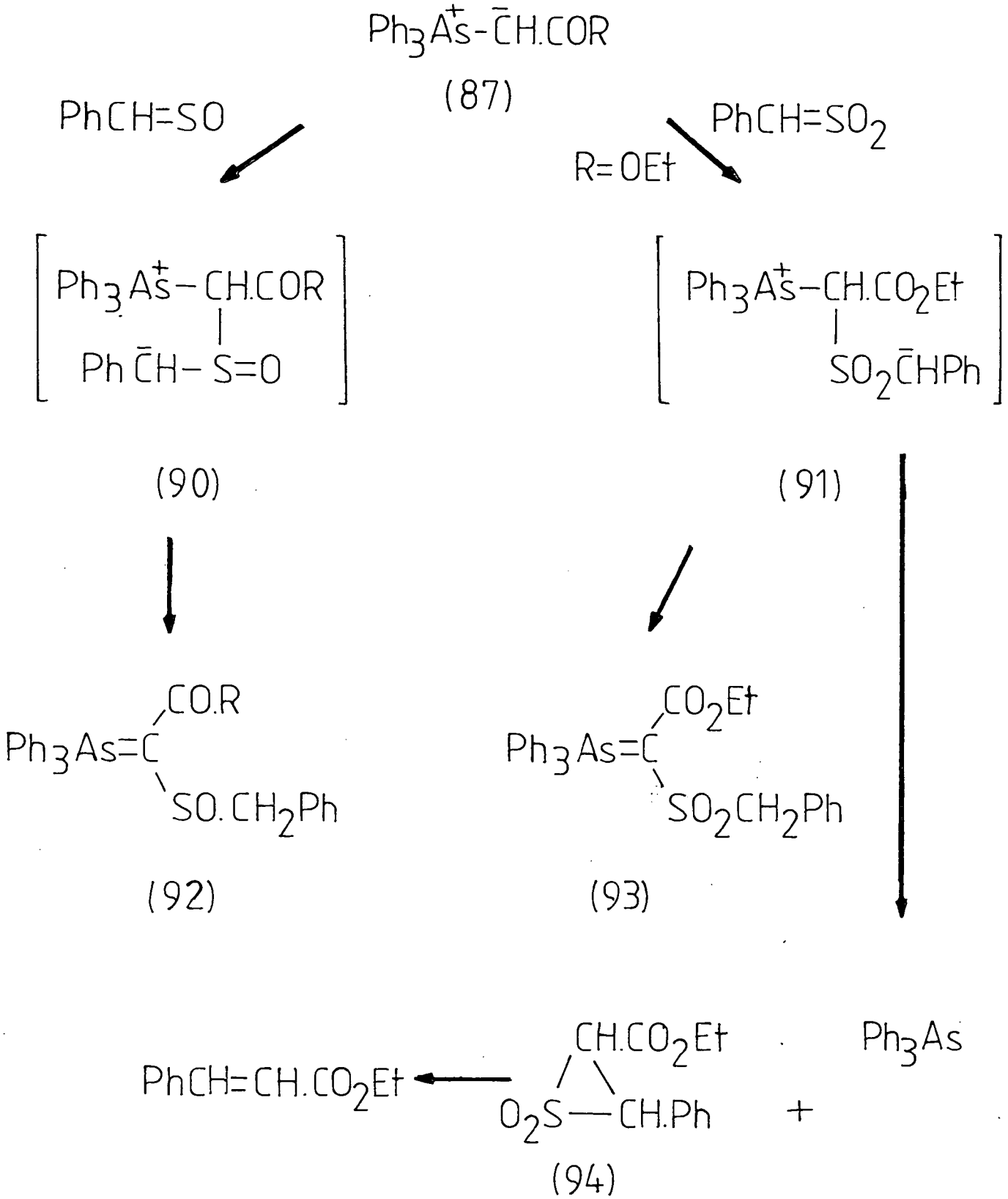
Scheme Twentyfour

The authors proposed that the rearrangement of the enol benzoate involved the conversion of a kinetically controlled product (86) to the thermodynamically controlled product (85). This accords with the observations of Chopard and co-workers[54] for the corresponding triphenylphosphonium phenacylide system.

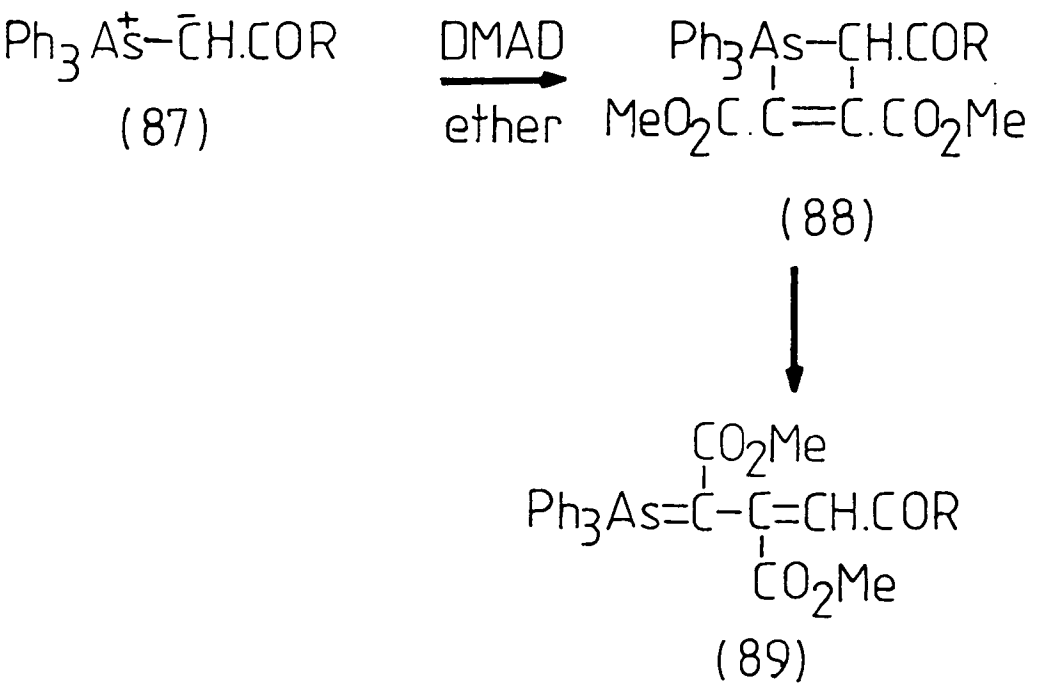
Ciganek[50] has reported that reaction of triphenylarsonium carbomethoxymethylide (24a) with methyl chloroglycoxylate leads to C-acylation exclusively. Such behaviour can be attributed to less enolate character in ester ylides compared with keto ylides[53] which undergo both C- and O-acylation depending on the reagent.

Recently, Tewari and Nagpal[48] have prepared several stabilised arsonium ylides by reaction of triphenylarsonium benzylide with acid chlorides or acid anhydrides.

Several other transylidation reactions of arsonium ylides have been reported using reagents other than alkyl or acid chlorides. For example, Trippett and Walker[30] showed that the carbonyl stabilised ylides (87, R=OEt, p-BrC_6H_4) reacted with dimethyl acetylenedicarboxylate to give stabilised ylides (89), presumably via a 4-membered cyclic transition state (88) as shown in Scheme Twentyfive. This mechanism is similar to that proposed by Hendrickson[88] and Bestmann[89] for the reaction between carbonyl stabilised phosphonium ylides and dimethyl acetylenedicarboxylate in aprotic solvents.



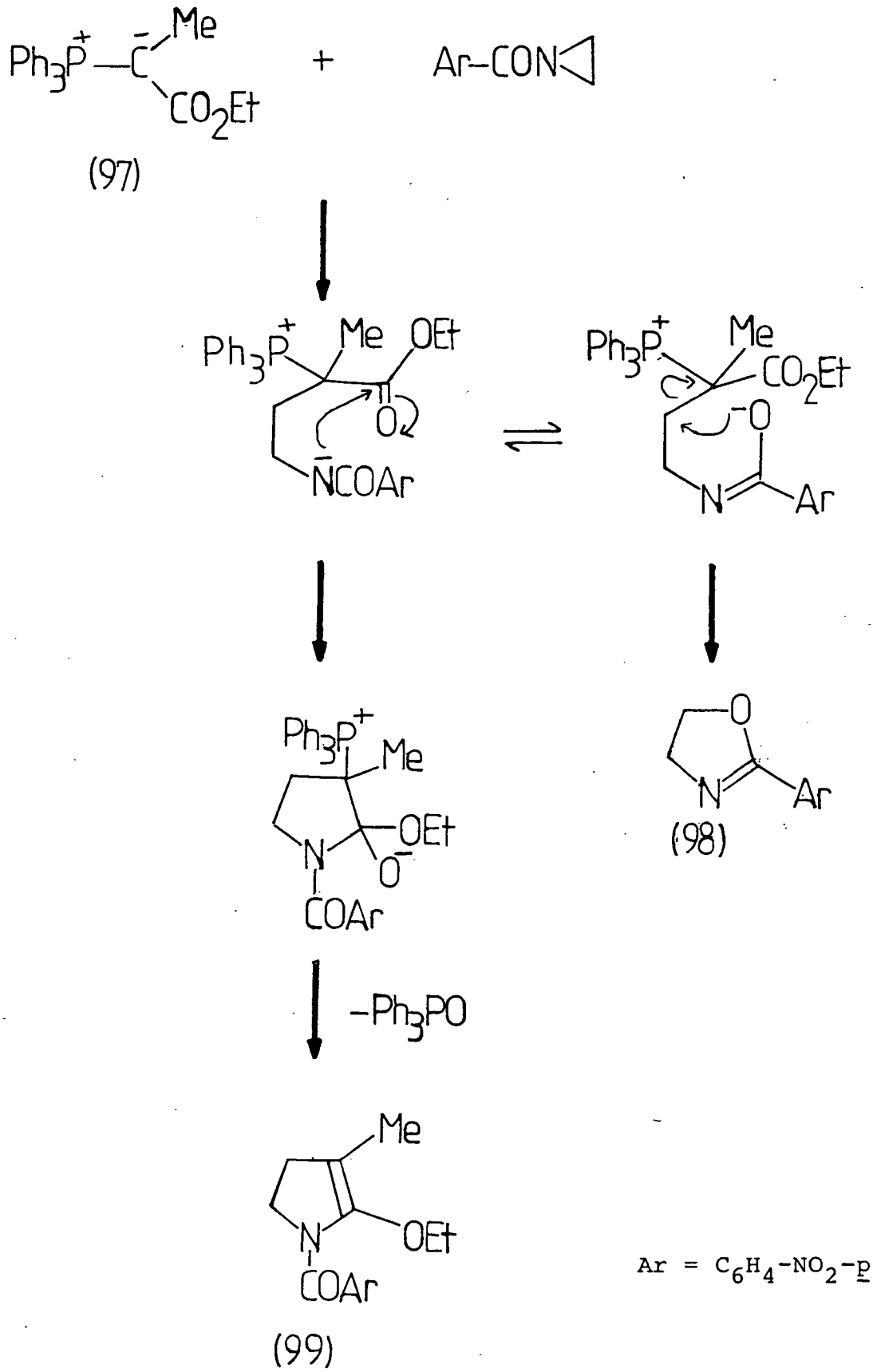
Scheme Twentysix



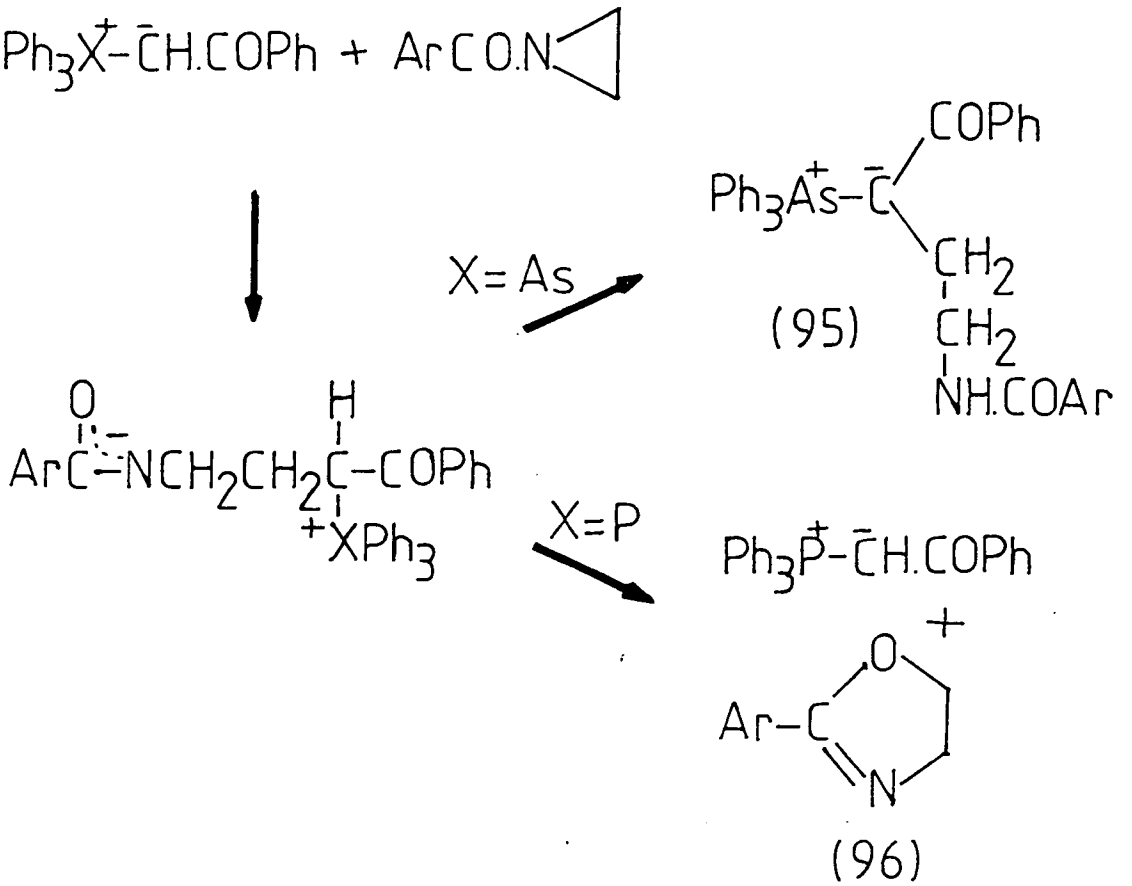
Scheme Twentyfive

The ylide (87, R = p-BrC_6H_4) also reacts with phenylsulphine to give the stable arsonium ylide (92), apparently by proton transfer in the initially formed adduct (90). Similarly, the ylide (87, R=OEt) reacts with phenylsulphene to give ethyl cinnamate, triphenylarsine, and the stable ylide (93). In this case, the cinnamate is presumably formed via the trans-episulphone (94) (Scheme Twentysix).

Heine and Wachob[47] have reported that the reaction between triphenylarsonium phenacylide and 1-p-nitrobenzoylaziridine in boiling toluene gives rise to (95). This course of reaction contrasts markedly with that for the corresponding phosphonium ylide, which acted as a catalyst, yielding the oxazoline (96) as shown in Scheme Twentyseven.



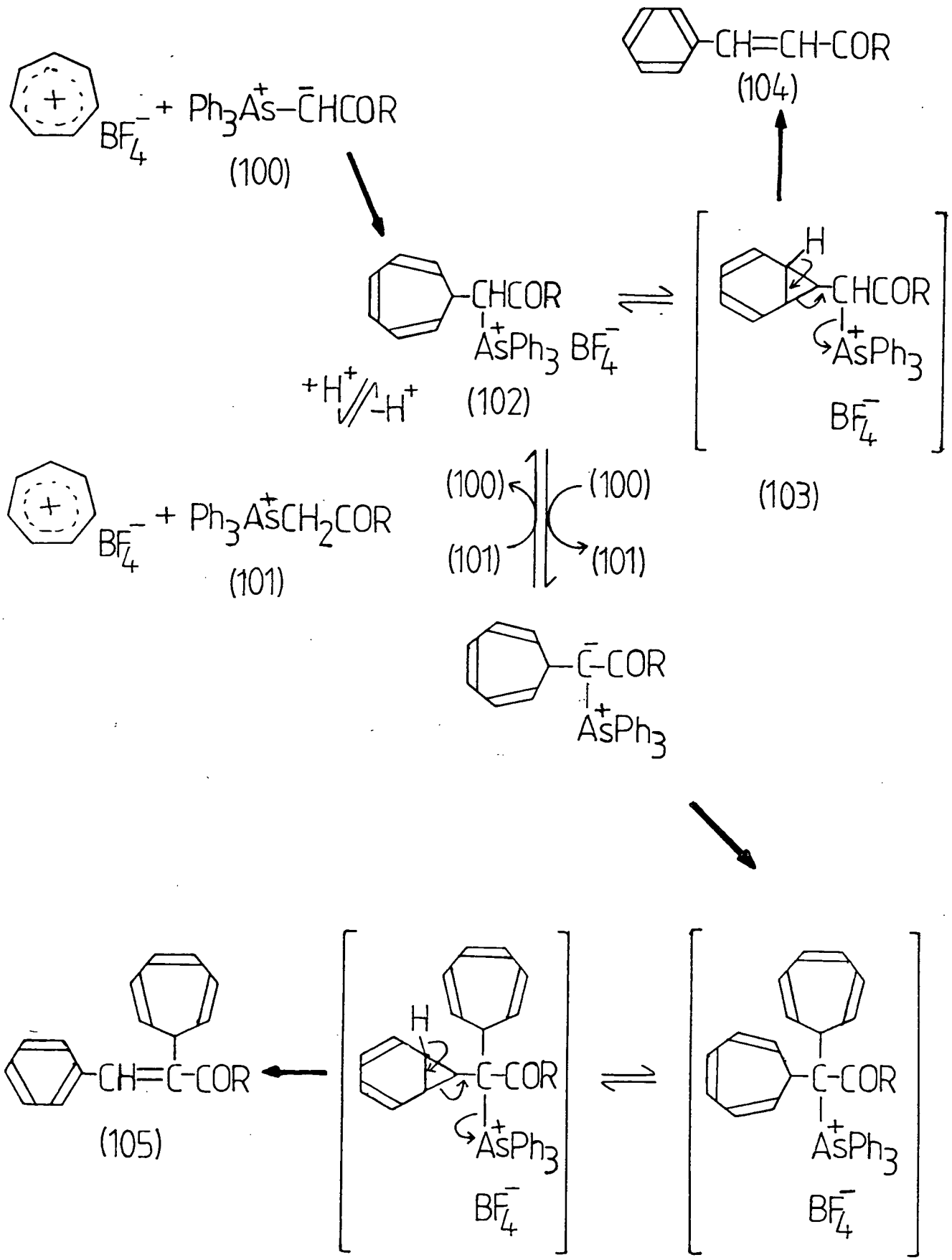
Scheme Twentyeight



Scheme Twentyseven

However, it is worth noting that the same reaction with triphenylphosphonium carbomethoxymethylide follows a different course, and gives rise to a new ylide corresponding to (95)[94]. It is also of interest that reaction of 1-p-nitrobenzoylaziridine with triphenylphosphonium α-carboethoxyethylide (97) yields a small quantity of the oxazoline (98) together with the pyrroline (99) as the major product (Scheme Twentyeight).

Gaudiano and co-workers[95] have reacted a variety of stabilised arsonium ylides with tropyllium tetrafluoroborate (Scheme Twentynine). The only products obtained were triphenylarsine, (104, R=Ph, OMe) and (105, R=OMe), and although the arsonium salt (102) could not be isolated, its intermediacy was confirmed by n.m.r.

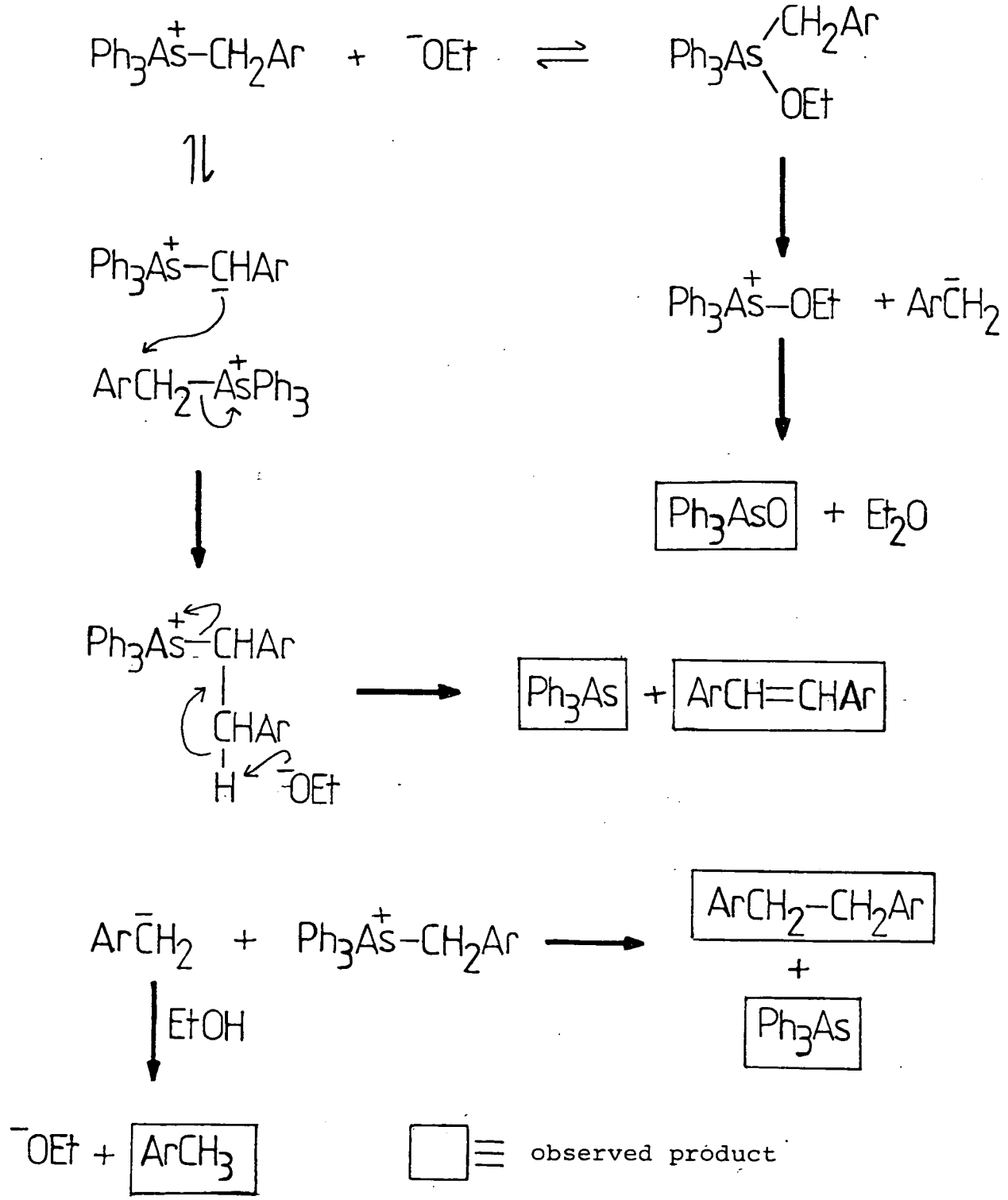


Scheme Twentynine

spectroscopy. Apparently, the styryl derivatives (104) are formed by the rearrangement of the arsonium salt (102) via its norcaradiene valence tautomer (103)[96-100]. The intermediate arsonium salt (102, R=OMe) underwent further reaction with tropyllium tetrafluoroborate as depicted in Scheme Twentynine).

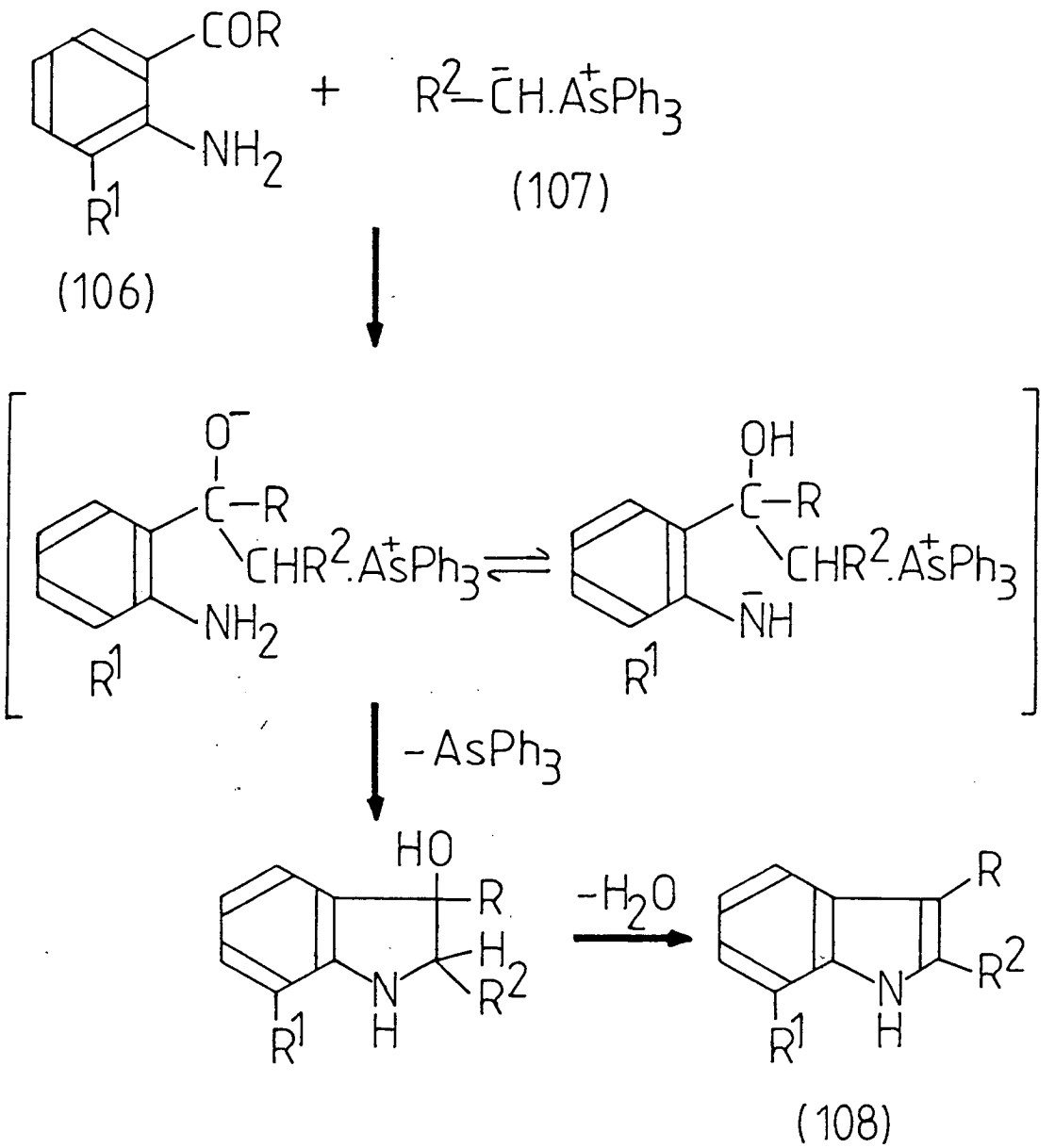
Like sulphonium ylides, arsonium ylides have proved to be very useful in the synthesis of heterocyclic compounds. For example, Trippett[30] has found that triphenylarsonium benzylide reacts with benzylidene-aniline to give 1,2,3-triphenylaziridine in 50% yield. In this reaction the ylide (15) resembles its sulphonium rather than its phosphonium analogue. The corresponding reaction of triphenylarsonium benzylide with benzylidene-m-nitroaniline afforded 1-m-nitrophenyl-2,3-diphenyl-aziridine together with N-benzyl-m-nitroaniline and m-nitroaniline. However, attempts to react triphenyl-arsonium p-nitrobenzylide, generated from its hydrobromide with ethanolic sodium ethoxide, with Schiff's bases gave only products of direct ethanolysis (Scheme Thirty).

In an extension of early work with sulphonium ylides[101,102] Gaudiano and co-workers[13] have prepared the indoles (108) from the reaction of non-stabilised arsonium ylides (107) with aromatic o-aminoketones (106). A plausible reaction mechanism is outlined in Scheme Thirtyone. Interestingly, they found that when the reaction between triphenylarsonium methylide and o-aminobenzophenone was run in cold tetrahydrofuran in the presence of lithium iodide, the normal pathway



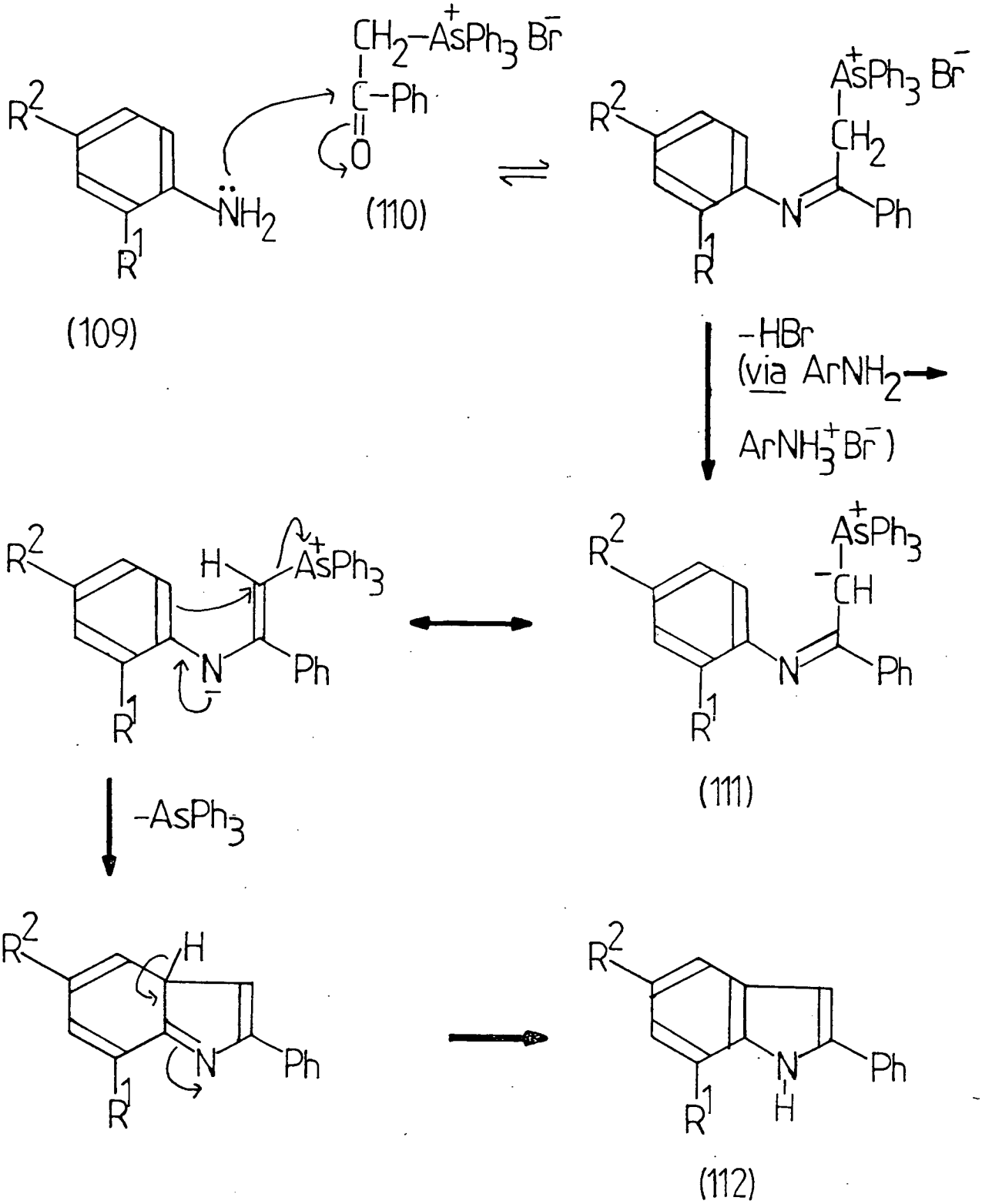
Ar = C_6H_4-NO_2-p

Scheme Thirty

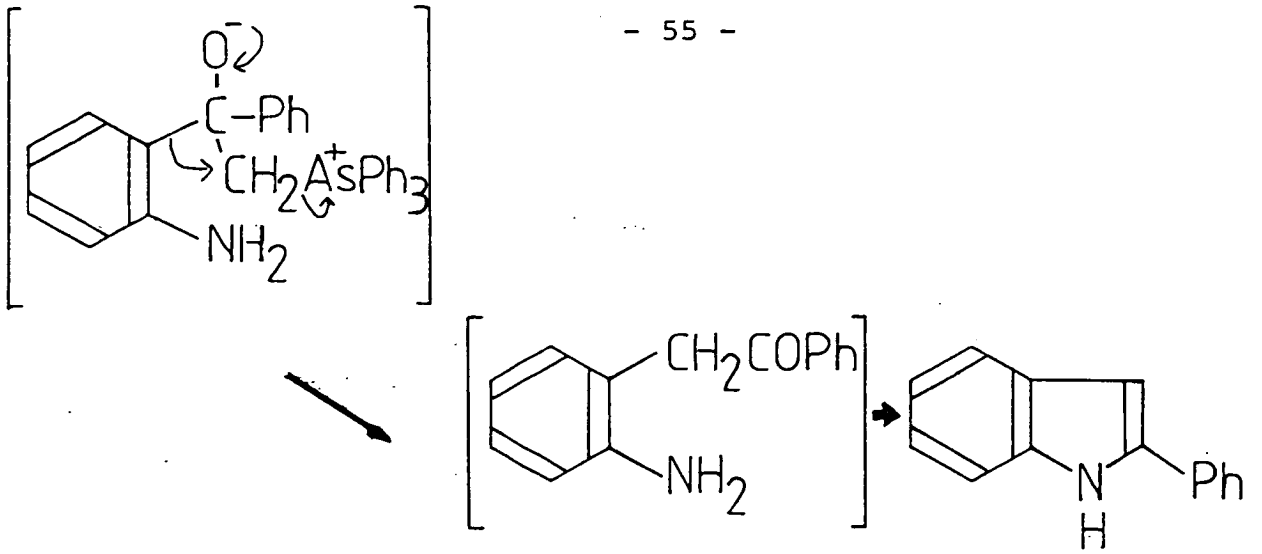


Scheme Thirtyone

was accompanied by a rearrangement to give 2-phenylindole. Apparently, under such conditions the nucleophilicity of nitrogen and oxygen is lowered, thereby favouring the alternative rearrangement pathway as shown in Scheme Thirtytwo.



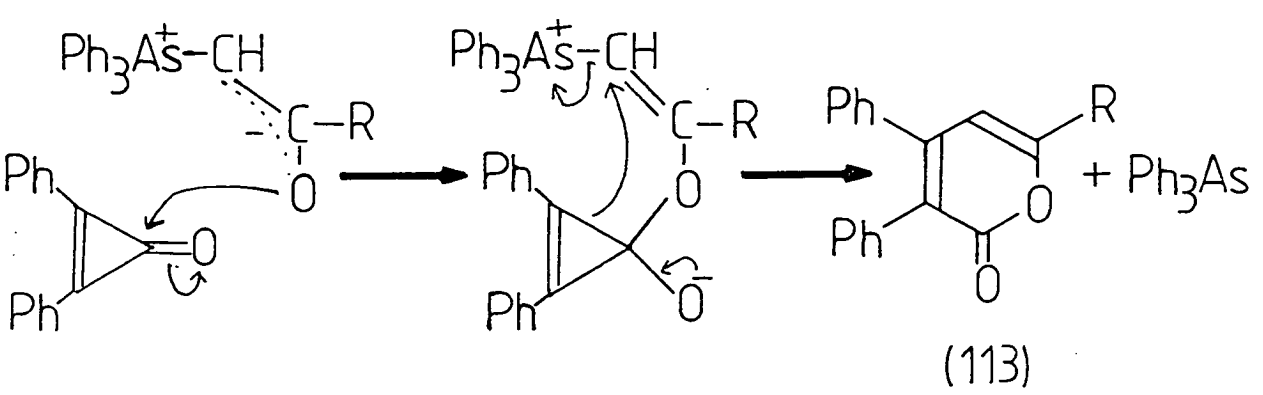
Scheme Thirtythree



Scheme Thirtytwo

An alternative indole synthesis has been reported by Bansal and co-workers[103,104] who found that the reaction between phenacyltriphenylarsonium bromide and anilines (109) in boiling N,N-dimethylaniline furnished the corresponding 2-phenylindole (112). They proposed a mechanism involving initial nucleophilic addition of the aniline to the carbonyl group of the arsonium salt (110) followed by proton abstraction to give the ylide (111) which ejected triphenylarsine as shown in Scheme Thirtythree.

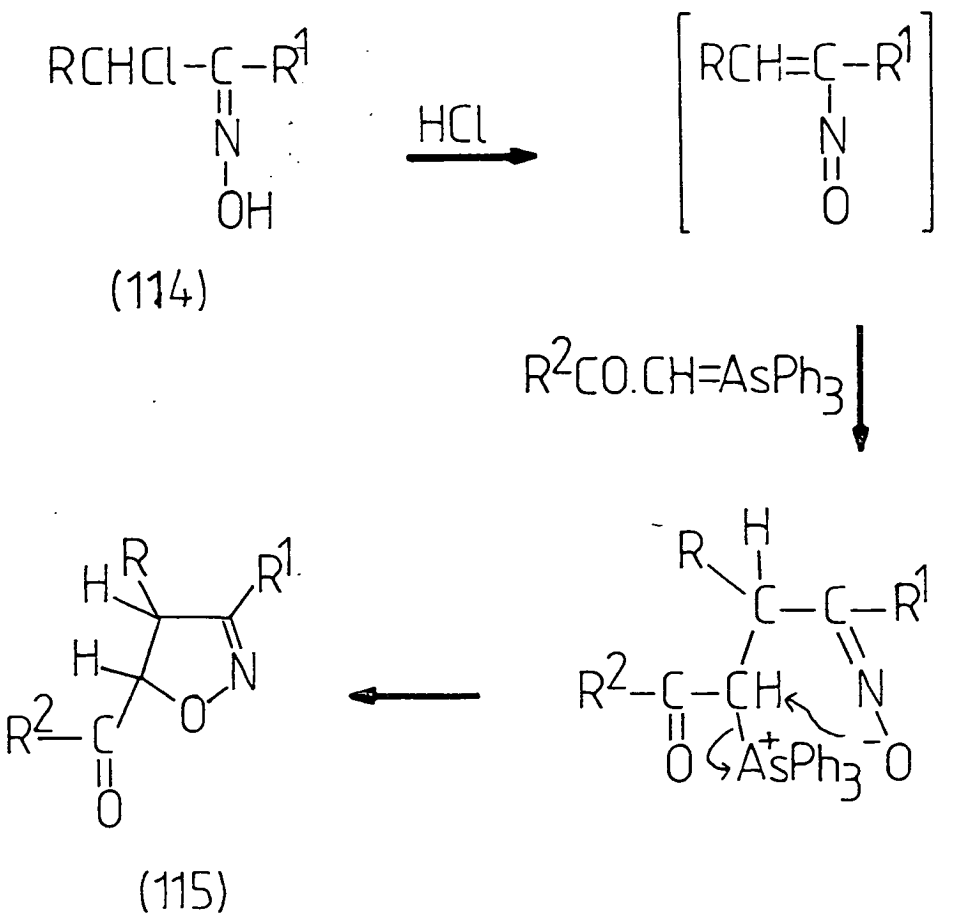
Gosney and Lloyd[40] have obtained α-pyrones (113) from the reaction of stabilised ylides with diphenylcyclopropenone, apparently via the mechanism shown in Scheme Thirtyfour.



(113)

Scheme Thirtyfour

In a further study of the use of stabilised arsonium ylides in heterocyclic synthesis, Gaudiano and co-workers[14] reported the formation of trans-5-acyl-Δ^2-isoxazolines (115) from the reaction of α-chlorooximes (114) with keto-stabilised triphenylarsonium ylides (Scheme Thirtyfive). A similar reaction occurred with keto-stabilised dimethylsulphonium ylides, but it is of interest to note that the analogous reaction with triphenylphosphonium phenacylide[14] afforded a complex mixture of compounds which could not be resolved. In this instance, arsonium ylides resemble sulphonium rather than phosphonium ylides, in accord with earlier observations[13,30,105].

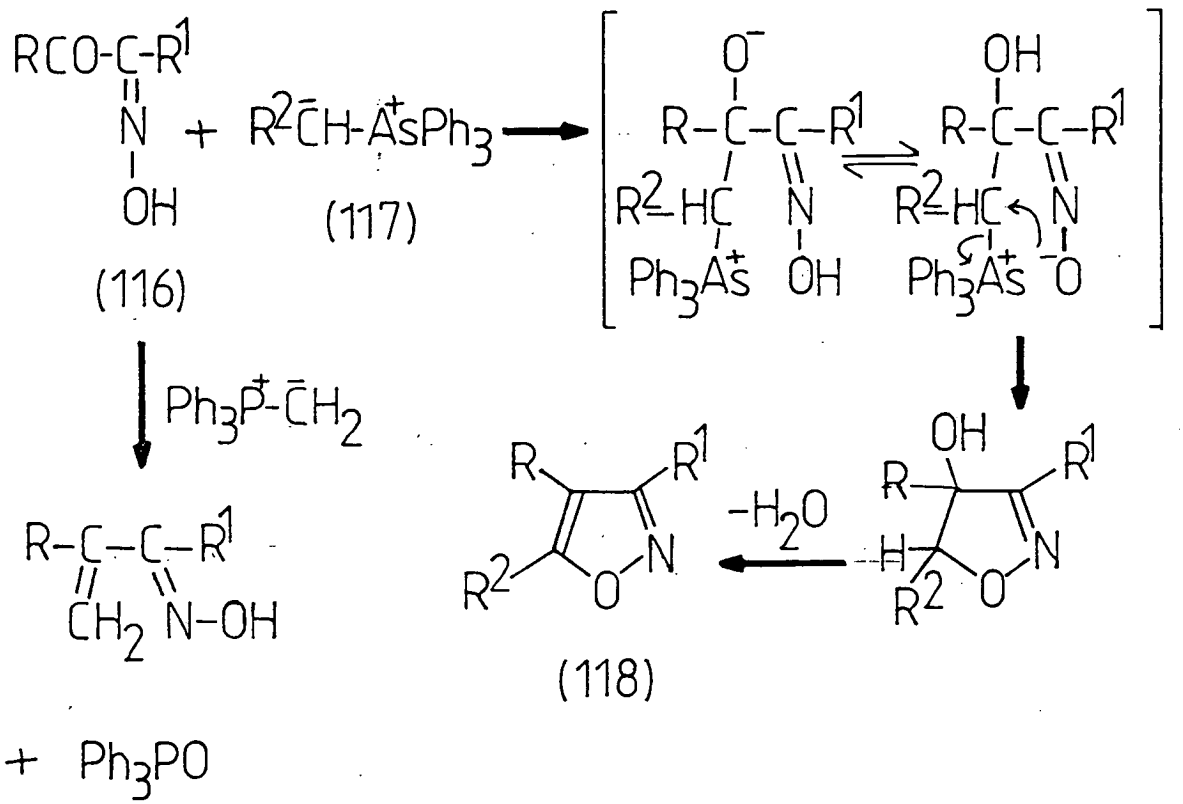


(114)

(115)

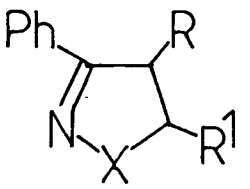
Scheme Thirtyfive

In a related study, isoxazoles (118) have been prepared by the reaction of α-isonitrosoketones (116) with reactive ylides (117) as shown in Scheme Thirtysix[15]. This pathway is analogous to that found for the corresponding sulphonium ylides, but different to that for phosphonium ylides which give the normal Wittig reaction product[15].



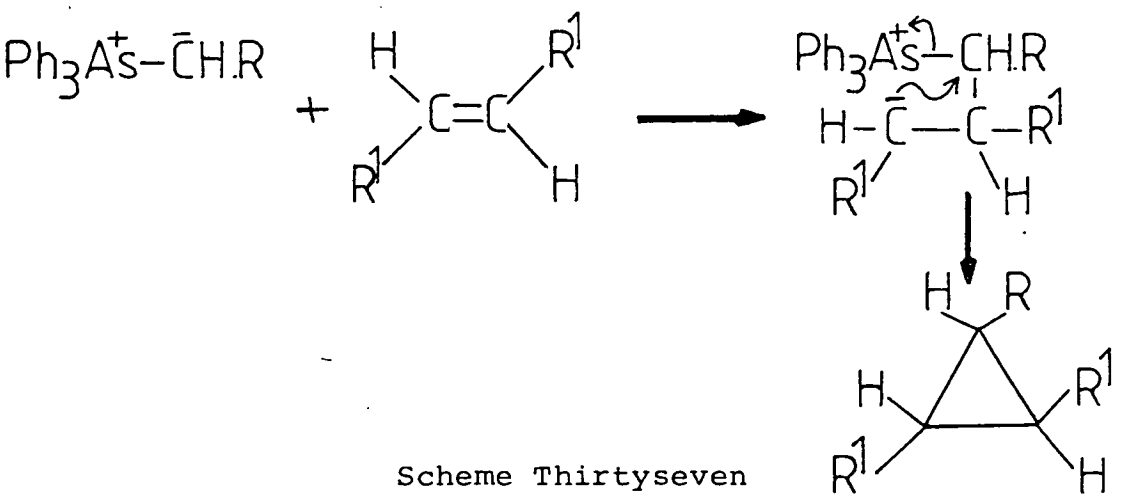
Scheme Thirtysix

Gaudiano and his co-workers[106] have also obtained isoxazoles (119, X=O) and pyrazoles (119, X=NR^2) from the reaction of the reactive ylide, triphenylarsonium methylide (30), with nitrile oxides and nitrile imines, respectively.



(119)

Finally, it is worth noting that both stabilised and reactive ylides have been utilised in the synthesis of cyclopropanes from activated olefins. Thus triphenylarsonium methylide yielded 1-aroyl-2-phenylcyclopropanes with β-aroylstyrenes[30], whilst keto-stabilised ylides reacted with more activated olefins, such as trans-dibenzoylethylene, to yield cyclopropane derivatives[12,107] (Scheme Thirtyseven). Interestingly, triphenylarsonium benzylide failed to react with stilbene[82].



Scheme Thirtyseven

1.4.2 Hydrolysis of arsonium ylides

From the meagre information available it appears that arsonium ylides are capable of hydrolysis to form an arsine and a hydrocarbon.

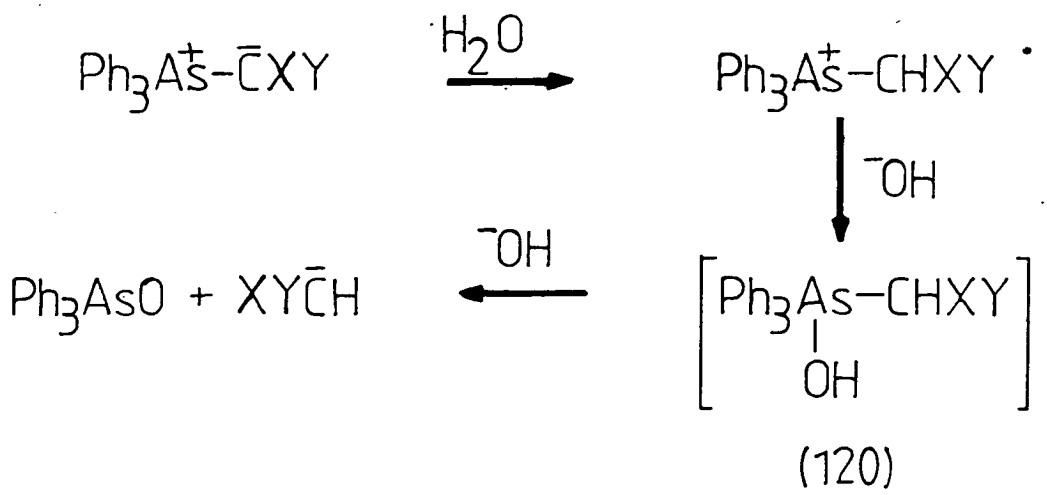
The conditions necessary to effect this cleavage appear to vary widely depending on the structure of the ylide, and only the more stable arsonium ylides are recovered unchanged in the presence of moisture.

The first hydrolysis of an arsonium ylide was reported in 1953 by Wittig and Laib[29] who found that solutions of trimethylarsonium fluorenylide (34, X=Me) underwent rapid hydrolysis on exposure to moisture to give fluorene and trimethylarsine oxide. By contrast, the phenyl analogue (17) was shown by Johnson[11] to be stable under these conditions, but it did hydrolyse when heated under reflux with ethanolic sodium hydroxide over long periods of time.

Several years later, Nesmeyanov[18] observed that the stabilised ylide triphenylarsonium phenacylide (22) underwent hydrolysis in acetophenone and triphenylarsine oxide on warming in aqueous ethanol. Likewise, Lloyd and Gosney[40] showed that the more stable triphenylarsonium p-nitrophenacylide (23) was hydrolysed readily to triphenylarsine oxide and p-nitroacetophenone when stirred with silica gel in benzene. By way of contrast, the β-diketo compounds (61), also investigated by these authors, were recovered unchanged even after heating under reflux in ethanolic sodium hydroxide[40].

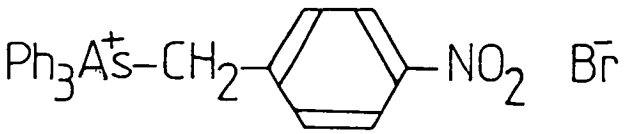
No studies have been undertaken to ascertain the mechanism of these hydrolyses, but Johnson[58] has speculated that they probably proceed in a manner analogous to that envisaged for phosphonium ylides[108] and involve ejection of the most stable carbanion from

the pentacovalent intermediate (120) (Scheme Thirtyeight).



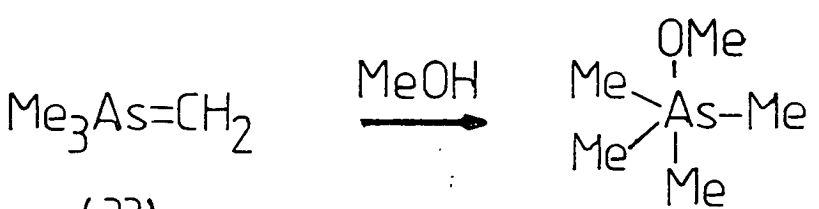
Scheme Thirtyeight

Some information regarding the hydrolysis of arsonium ylides can be gleaned from the detailed study of the ethanolysis of p-nitrobenzyltriphenylarsonium bromide (121) by Trippett and Walker[30] (Scheme Thirty). In this instance, the pathway followed differed from that observed for the corresponding phosphonium salt[109]. Whereas the latter gave only p-nitrotoluene, diethyl ether and triphenylphosphine oxide, the corresponding arsonium salt afforded 4,4^1-dinitrobibenzyl, triphenylarsine, 4,4^1-dinitrostilbene, p-nitrotoluene, diethyl ether and triphenylarsine oxide. This difference in behaviour presumably reflects the relative strengths of the P-O versus As-O bonds. Apparently, the weaker As-O bond does not influence the ethanolysis of the arsonium salt (121) to the same extent as observed for the corresponding phosphonium salt, whose behaviour closely parallels the hydrolysis reaction.



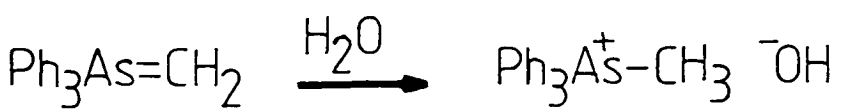
(121)

The necessity for a stable carbanion to be ejected in the solvolysis is evidenced by the reaction of trimethylarsonium methylide (33) with methanol to afford the arsorane (122)[110]. In this instance, arsenic-oxygen bond formation offers insufficient driving force to lead to dissociation by loss of a methyl carbanion.



(33) (122)

In marked contrast to this stability, triphenylarsonium methylide (30) reacts with water to give methyltriphenylarsonium hydroxide (123)[25].



(30) (123)

In summary, it appears that stabilised arsonium ylides can be hydrolysed to an arsine oxide and a hydrocarbon, but in the absence of a suitable carbanion for ejection as in the case of reactive ylides, an alternative pathway may be followed.

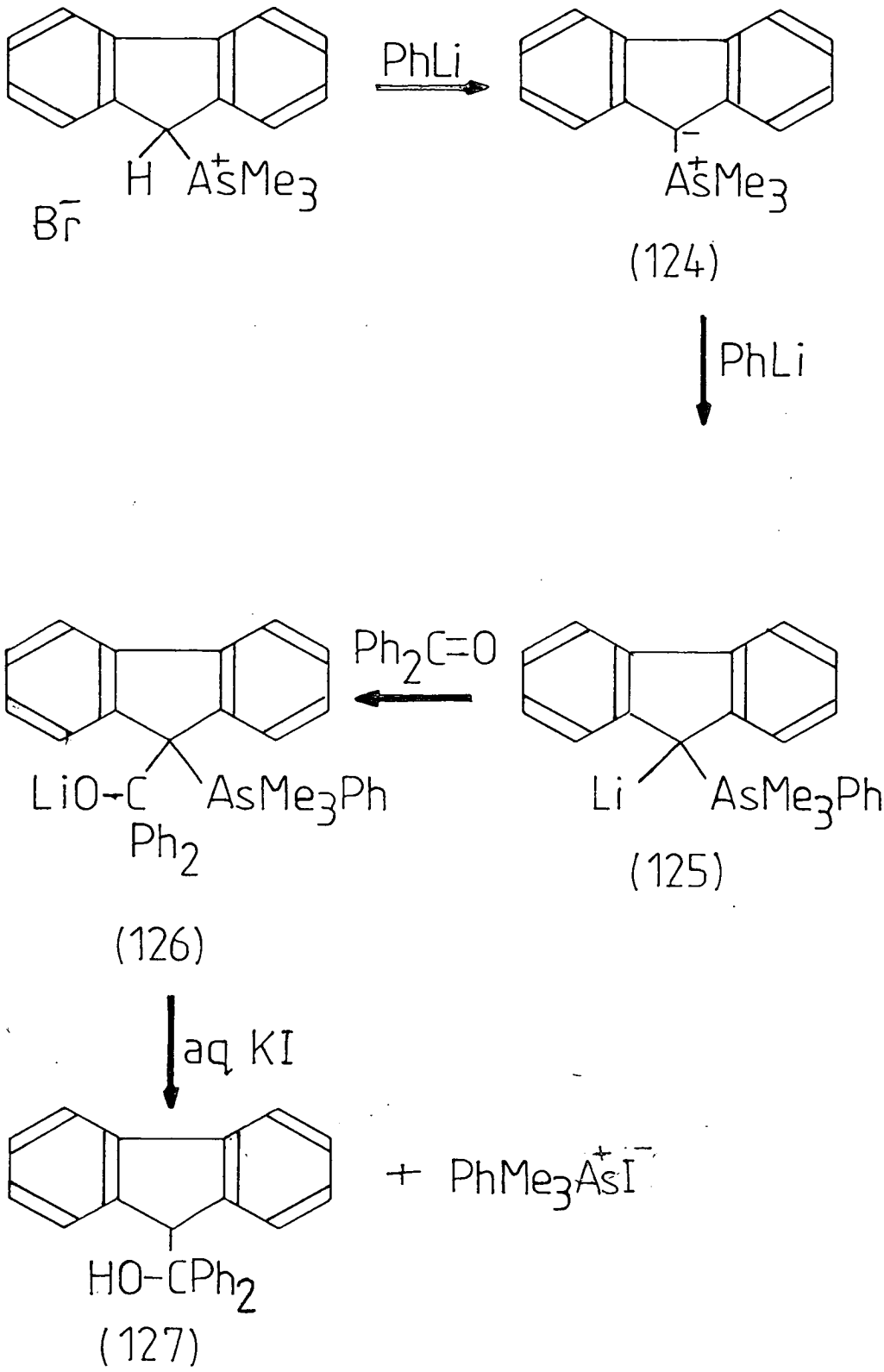
1.4.3 Reactions with carbonyl compounds

(i) Historical

The most important aspect of ylide chemistry is without doubt their reaction with carbonyl compounds, and considerable effort has been extended in this direction with phosphonium[58,111] and sulphonium ylides[6,112]. By comparison, little work has been done with arsonium ylides, and most developments in this field have occurred within the last two decades, mainly as an extrapolation of the Wittig synthesis of olefins.

The first record of a reaction between an arsonium ylide and a carbonyl compound was in 1937 by W. Heffe, a student of Krohnke's who reported in his dissertation that phenacyltriphenylarsonium bromide reacted with benzaldehyde in the presence of sodium hydroxide to form benzalacetophenone[113]. The reaction was not elaborated and remained isolated in the literature until the advent of the Wittig reaction aroused interest in the chemistry of ylides, in general.

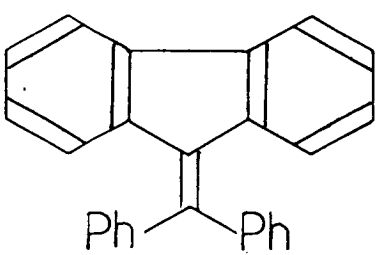
The first published report of a reaction between an arsonium ylide and a carbonyl compound occurred in 1953 when Wittig and Laib[29] prepared solutions of trimethylarsonium fluorenylide (124) and found that



Scheme Thirtynine

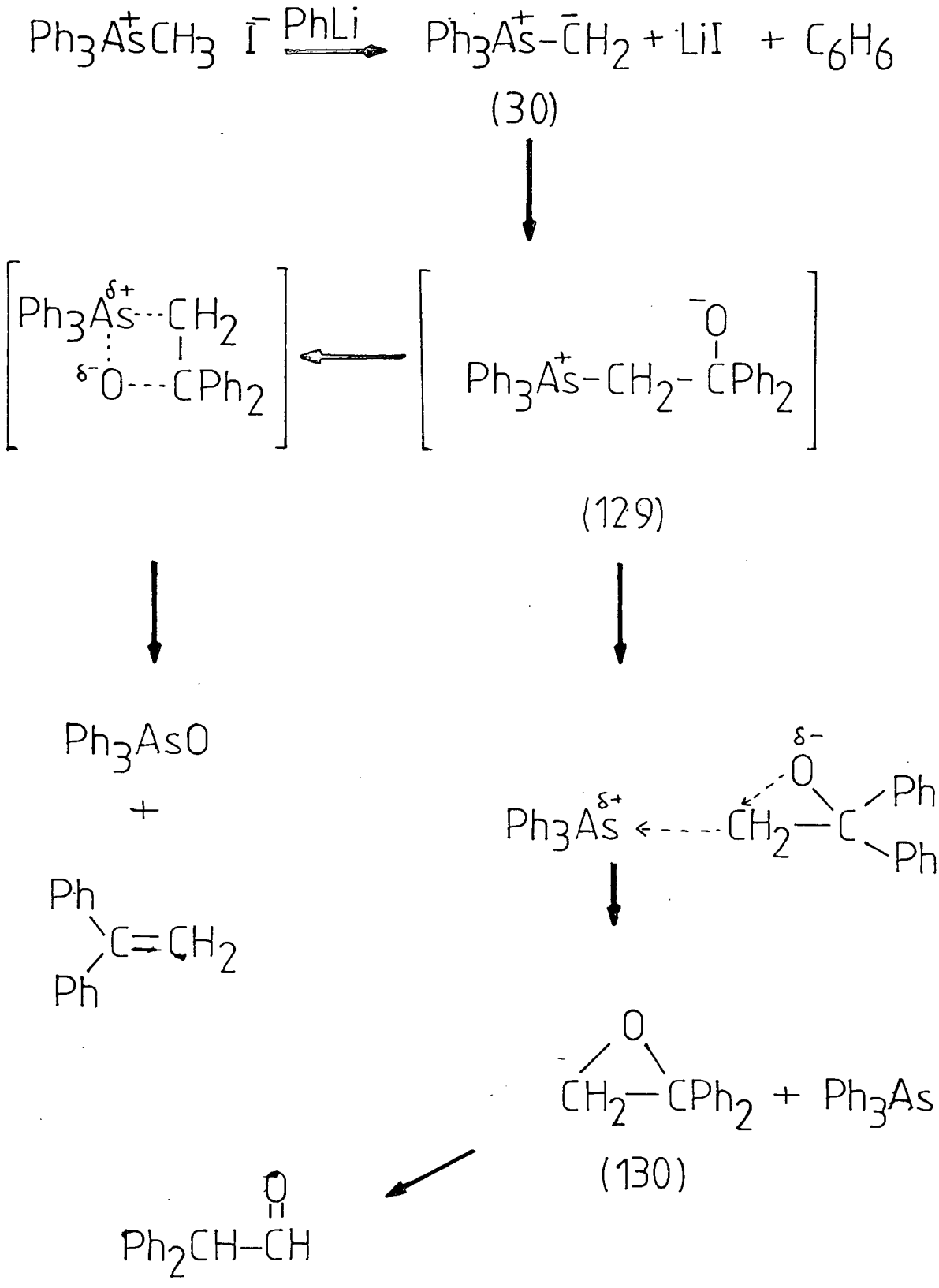
reaction with benzophenone afforded phenyltrimethylarsonium iodide and 9-fluorenyldiphenylcarbinol (127). The latter was thought to be formed by a simple carbanion addition to benzophenone as shown in Scheme Thirtynine.

This mechanistic proposal is without proof or precedent, and a proper evaluation of the work is not possible since a molar excess of phenyllithium was used to generate the ylide, despite the incipient addition of a ketone. Moreover, the carbinol product (127) was not identified directly, but dehydrated to the characterisable benzhydrilidene fluorene (128) which is the expected Wittig product.



(128)

After a lapse of several years, Henry and Wittig[9] published an account of the reaction between the simple arsonium ylide, triphenylarsonium methylide (30) and benzophenone. The ylide was generated in ethereal solution by treatment of its hydrobromide or iodide with an equivalent quantity of phenyllithium. An equimolar amount of ketone was then added and the mixture heated at 60°C for 12 hr. Subsequent hydrolysis with mineral acid afforded a mixture of four products which were identified as triphenylarsine (68%), diphenyl-

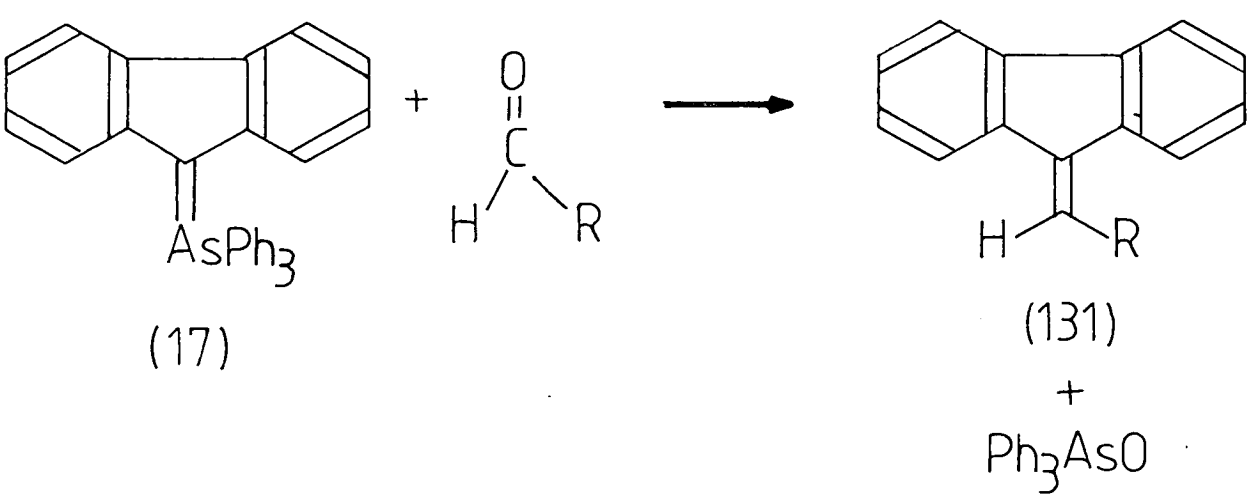


Scheme Forty

acetaldehyde (64%), triphenylarsine oxide (2%), and 1,1-diphenylethylene (1%). The first two products were obtained in approximately equimolar amounts, as were the latter two, indicating that the reaction proceeded by two different pathways via the intermediacy of the betaine (129) (Scheme Forty). It was suggested that the diphenylacetaldehyde was formed by the rearrangement of the initially formed epoxide (130).

Whilst no evidence was offered by Wittig and Henry[9] to substantiate the intermediacy of the epoxide, an adequate analogy for its formation did exist in the earlier findings of Johnson and LaCount[7,114] who isolated epoxides from the reaction of sulphonium ylides with carbonyl compounds.

Contrary to these observations, Johnson[11] described the preparation of the stabilised arsonium ylide triphenylarsonium fluorenylide (17) and discovered that it reacted with a series of benzaldehydes in typical Wittig fashion to produce the fluorenylidene derivatives (131) and triphenylarsine oxide. No evidence was found of any ketonic products as might have been expected on the basis of Wittig and Henry's results.

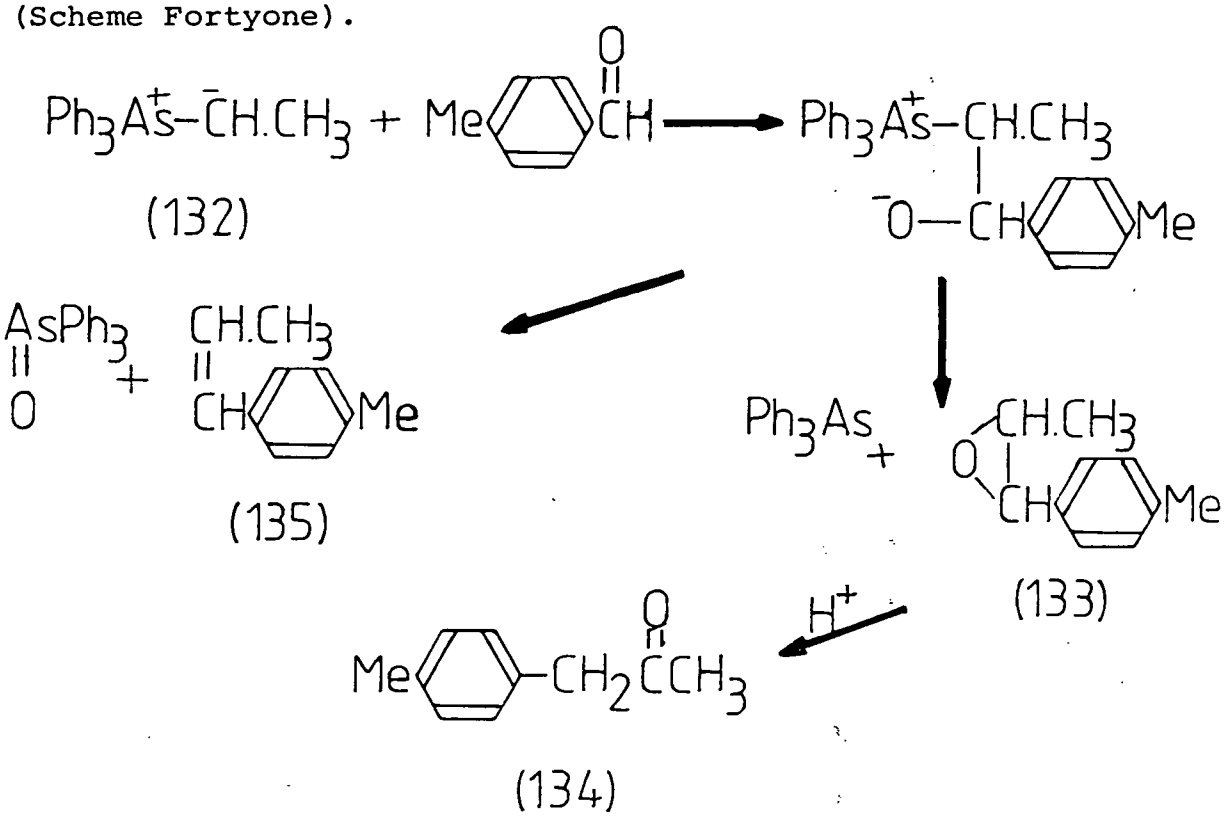


(17) (131)

Since then, the reactions of several other stabilised arsonium ylides with carbonyl compounds have been examined and in all cases the ylides exhibited similar behaviour. For example, Huang and co-workers[19] have shown that triphenylarsonium carbomethoxymethylide (24a) reacts with several aromatic aldehydes and ketones to afford the methyl ester of the corresponding α,β-unsaturated acids in good yield. At the same time, Nesmeyanov and co-workers[115] and, later, Johnson and Schubert[12] reported that the reaction of triphenylarsonium phenacylide (22) with p-nitrobenzaldehyde afforded only p-nitrobenzalacetophenone and triphenylarsine oxide. The Russian group[116] also prepared other stabilised arsonium ylides and found that their reactions with aldehydes proceeded in the same way to yield olefins exclusively. More recently, Lloyd and Singer[37] showed that the stabilised triphenylarsonium cyclopentadienylides also react with aldehydes in the normal way to form the corresponding fulvenes in high yield.

Conclusive evidence that arsonium ylides could follow different reaction pathways depending on their stability was obtained by Maccioni and Secci[116] who found that the non-stabilised ylide, triphenylarsonium ethylide (132) reacted readily with p-tolualdehyde to give p-xylylmethylketone (134) in high yield (95%) and only a small amount of the normal Wittig product, trans-1-propenyl-4-methylbenzene (135). It was suggested that the product (134) was formed via an epoxide intermediate (133) which rearranged during

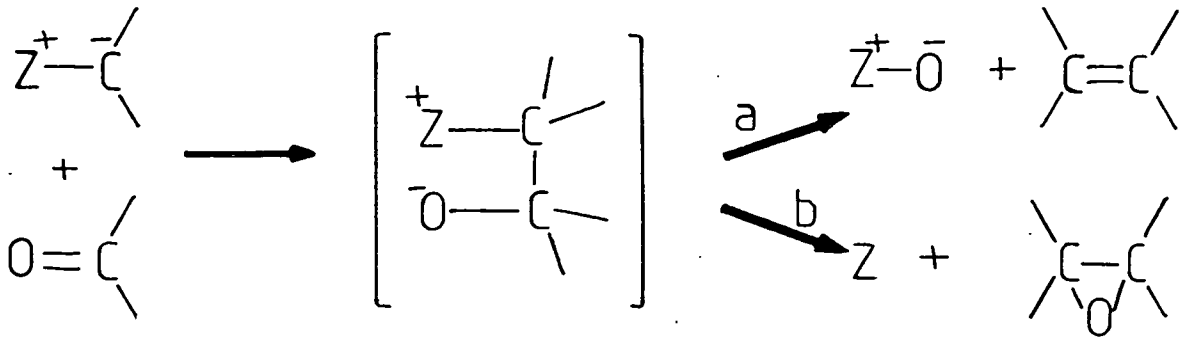
work-up rather than during the course of the reaction (Scheme Fortyone).



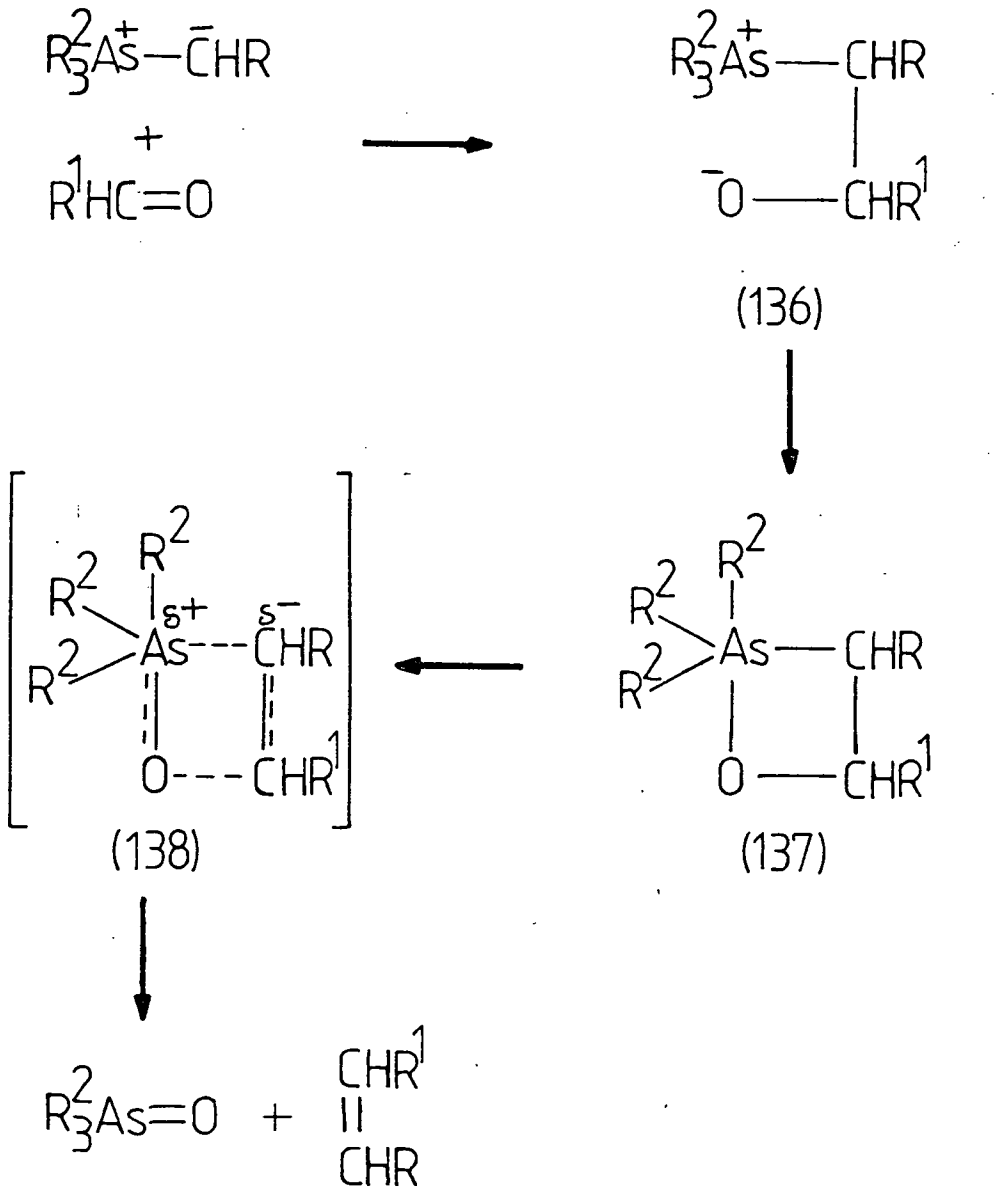
Scheme Fortyone

The proposal that epoxides are the primary product from reactive arsonium ylides and aldehydes received further support from Johnson and Martin[10] who isolated p-nitrostilbene oxide from the reaction of triphenylarsonium benzylide with p-nitrobenzaldehyde. Four products in all were obtained; a 1:1 mixture of triphenylarsine oxide and p-nitrostilbene (21%), together with a 1:1 mixture of triphenylarsine and p-nitrostilbene oxide (32%) (Scheme Five). Significantly in this case the work-up of the reaction did not involve acid hydrolysis.

On the basis of these results and previous evidence, Johnson and Martin[10] suggested that arsonium ylides held a position intermediate between phosphonium



Scheme Fortytwo



Scheme Fortythree

and sulphonium ylides in the course of their reaction with carbonyl compounds (Scheme Fortytwo). They argued that the conjugation and stabilisation afforded by the ylide substituents (R) and the carbonyl substituents (R^1) to an incipient double bond in the transition state (138) should favour olefin formation (Scheme Fortythree). In the absence of such stabilisation epoxide formation might be expected to be the normal mode of reaction.

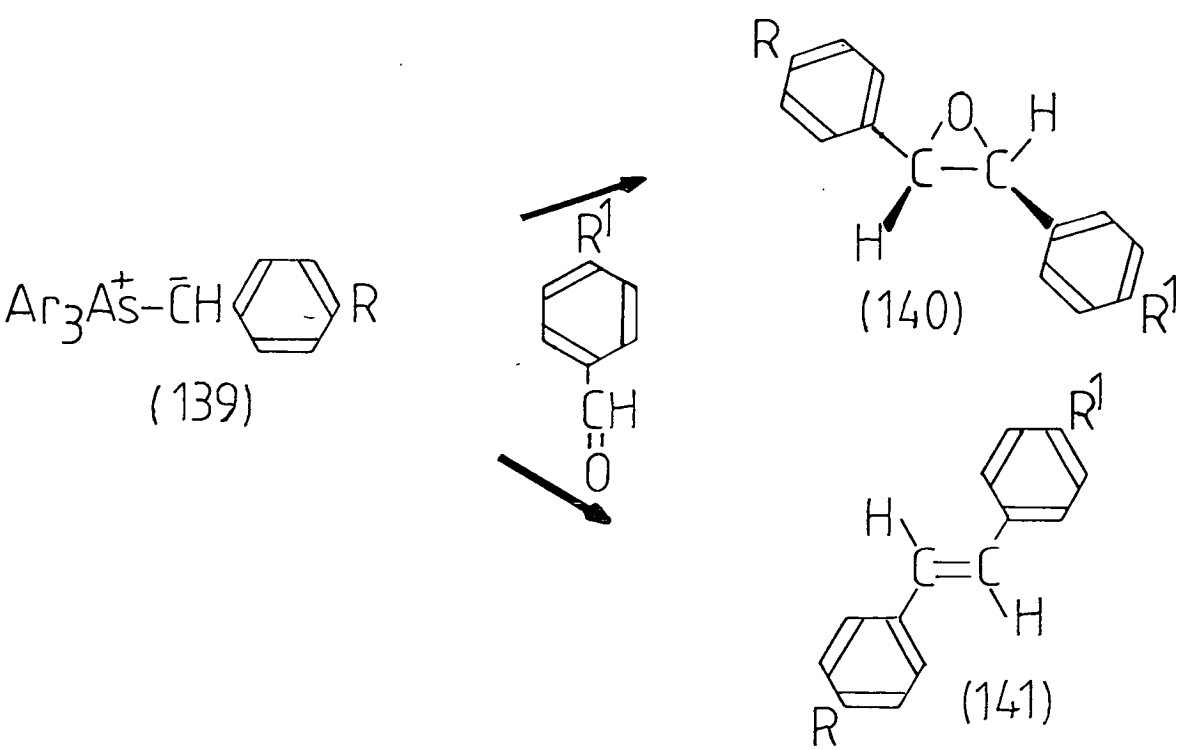
Prior to the work of Johnson and Martin, Nesmeyanov and co-workers[115] reported that the reaction between triphenylarsonium benzylide and benzaldehyde gave negligible yields of stilbene and triphenylarsine oxide, although triphenylarsine and other undisclosed products were obtained. From this result, and those of Johnson[11] and Wittig[9], the Russian workers asserted that stable arsonium ylides react with aldehydes in the normal way, whereas reactive ylides form a mixture of products.

Somewhat later, Johnson and Schubert[12] accounted for all the reactions of arsonium ylides with carbonyl compounds and came to the conclusion that stabilised ylides such as the phenacylide[12,115], carbomethoxy-methylide[19], fluorenylide[11] and cyclopentadienylide[37] give rise to olefins only, whereas non-stabilised ylides such as the methylide[9] and ethylide[116] afford mainly epoxides or their rearrangement products. They suggested that path b (Scheme Fortytwo) may be the 'normal' path as triphenylarsine is not an especially strong oxygen scavenger[50] as is triphenylphosphine.

The dichotomous behaviour of arsonium ylides towards carbonyl compounds was further investigated by Trippett[30] who examined the reactions of several arsonium ylides with aldehydes in ethanol. In no case were both olefin and epoxide obtained and in all cases only trans-olefin or trans-epoxide was detected. Trippett proposed that the determining factor for olefin formation was the presence of a grouping R which could stabilise an adjacent carbanion. It was argued that in the transition state (138) for olefin formation, the breaking of the As-C bond is in advance of other electron shifts and that the α-carbon bears a fractional negative charge (Scheme Fortythree). Stabilisation of this charge would lead to faster olefin formation. Corey and Kwiatkowski[117] have suggested a similar distribution of charge in the transition state for olefin formation from phosphonate carbanions.

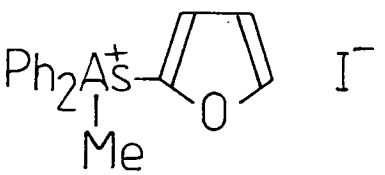
Recently Tewari and co-workers[31-34,118] have looked at the reaction between semi-stabilised arsonium ylides and carbonyl compounds. In most cases[31-33,118] only trans-olefination was observed but an anomaly did arise for the reaction between triphenylarsonium 1-bromo-2-naphthylmethylide (39, R=Br) and triphenylarsonium 2-naphthylmethylide (39, R=H) with carbonyl compounds[34]. Whereas the former ylide afforded olefin products, the latter ylide gave rise to epoxide products. This difference in products on going from (39, R=H) to (39, R=Br) can be attributed to the increase in stabilisation due to the o-bromo group of (39, R=Br), thereby favouring olefin formation.

By comparison with the literature available concerning the carbanion portion of arsonium ylides, there has been a paucity of reports on the effect of substituents at arsenic on the direction of the reaction between arsonium ylides and carbonyl compounds. Trippett[30] has reported that the ylides (139, Ar = p-$MeOC_6H_4$, Ph) reacted with benzaldehydes to give either epoxides (140, R=NO_2, R^1=NO_2, H) or an olefin (141, R=H, R^1=NO_2) in approximately equal yields (Scheme Fortyfour). In this connection it is noteworthy that use of tris-p-methoxyphenylphosphonium salts as precursors for phosphonium ylides so reduces the electropositive character of the phosphorus that elimination of phosphine oxide from the betaines is inhibited[119]. This was not so with the corresponding arsonium salts.

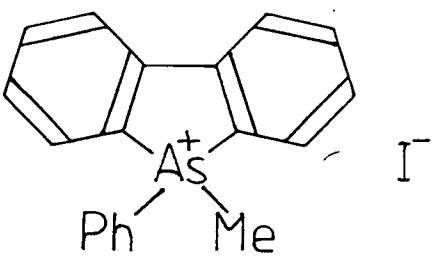


Scheme Fortyfour

In a further study, Allen and Jackson[120] investigated the steric and electronic effects of substituents at arsenic on the decomposition of arsonium betaines. Both 2-furyl(methyl)diphenylarsonium iodide (142) and 5-methyl-5-phenyldibenzarsolium iodide (143) on treatment with benzaldehyde and ethanolic sodium hydroxide gave exclusive formation of epoxide and tertiaryarsine. Significantly, neither the presence at arsenic of the electron-withdrawing 2-furyl substituent nor enclosure of the arsenic into the strained dibenz-arsolium ring system served to promote betaine collapse <u>via</u> attack of the betaine oxygen at the arsonium centre.



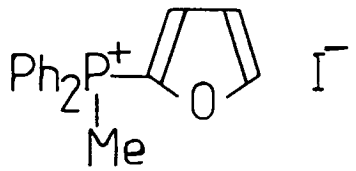
(142)



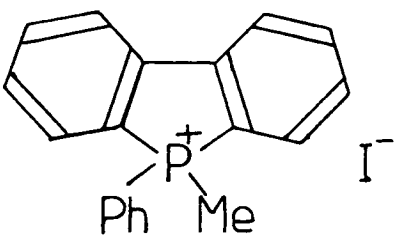
(143)

This was in marked constrast to the behaviour of the corresponding phosphonium betaines which collapsed to give only olefin products[121-123]. In the phosphorus cases betaine collapse is accelerated by the electron withdrawing 2-furyl substituent at phosphorus in (144) and by the relief of strain attendant on the formation of the spiro-oxaphosphorane (146) with (145). From the results of Allen and Jackson[120] it can be seen that the presence of an electron-withdrawing substituent at arsenic does not facilitate betaine collapse <u>via</u> nucleophilic attack

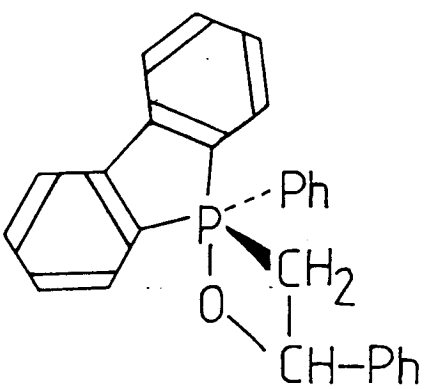
at arsenic, in contrast to the situation observed for the analogous phosphonium betaine. Rather, the absence of an electron-withdrawing substituent on the α-carbon is clearly the controlling influence, even when the arsonium centre is made more electropositive.



(144)



(145)

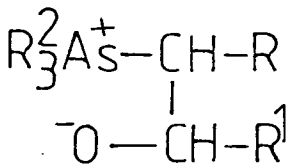


(146)

Gosney, Lillie and Lloyd[124] have also examined the effects of substituents at arsenic and obtained conclusive evidence to support the supposition that the nature of the arsonium group influences the course of the reaction between arsonium ylides and carbonyl compounds. They found that the presence of electron-donating substituents at the arsenic atom promoted the formation of alkene (Scheme Fortytwo; path a). From the results obtained, the authors concluded that the general reaction of arsonium ylides with carbonyl

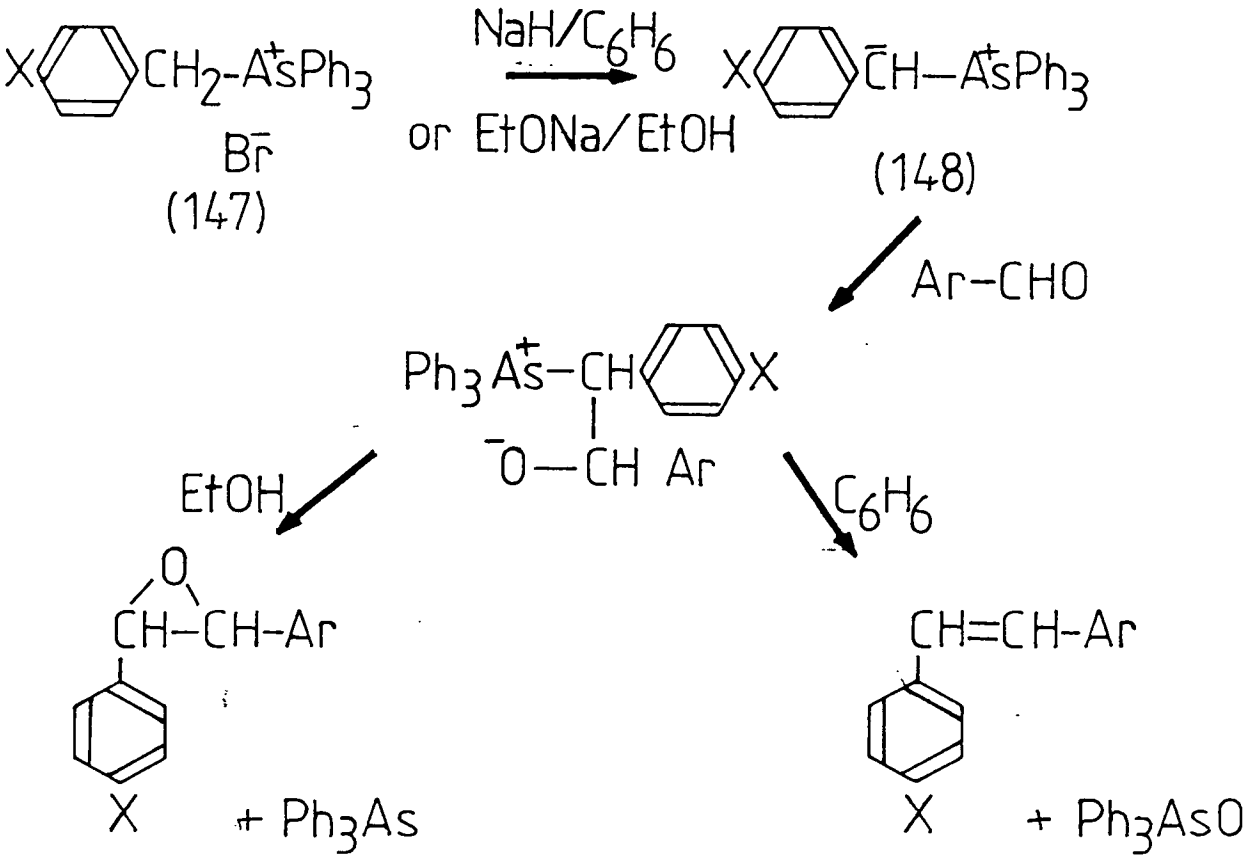
compounds is not solely related to the nature of the carbanion moiety, as previously assumed, but depends in part on the electronic character of the substituents at arsenic. The relative importance of the two effects was not accessible from the experimental evidence.

From the meagre information available it is apparent that decomposition of the betaine (136) can be influenced in several ways. The evidence suggests that electron-withdrawing groups R promote alkene formation[12,30] as do electron-donating substituents on the arsenic[124]. Presumably, an electron-donating substituent on the arsenic will promote epoxide formation.



(136)

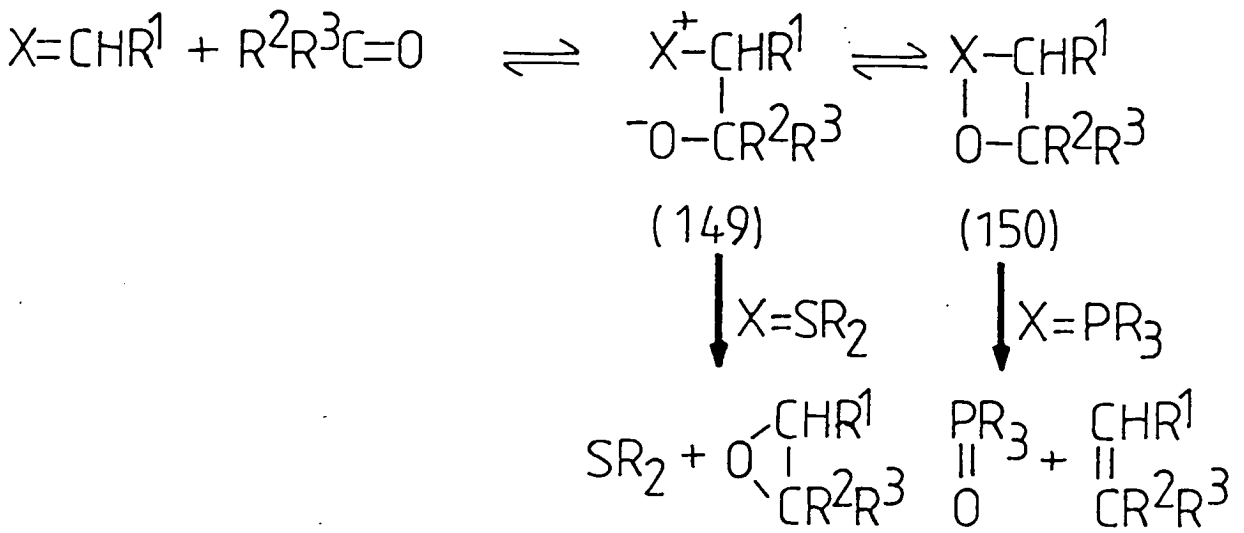
A further complicating factor is the question of solvent, and the nature of the generating base. Tewari and Chaturvedi[125] reported that reaction of ylides (148, X=H, Cl), generated from their salts using sodium hydride in benzene with aromatic aldehydes afforded exclusively olefins. Similarly, the same ylides, generated by sodium ethoxide in ethanol, afforded only epoxide products on reaction with aromatic aldehydes (Scheme Fortyfive). This illustrated that the base and solvent play an important role in dictating the exact path of the reaction of arsonium ylides with carbonyl compounds.



Scheme Fortyfive

(ii) Mechanism

As a result of extensive investigations it has been established that, in general outlines, the Wittig reaction proceeds via a betaine adduct (149) and thereafter by a cyclic rearrangement of electrons to give an olefin and phosphine oxide (Scheme Fortysix)[3,126]. With sulphonium ylides it is thought that the reaction commences as for the Wittig reaction but diverges at the second step to give an epoxide by displacement (Scheme Fortysix).[58] Since arsonium ylides can afford either an olefin or an epoxide, or a mixture of both, it is reasonable to assume that a two-step mechanism is involved also but that the two modes of betaine decomposition are in balance.



Scheme Fortysix

Wittig and Henry[9] were the first workers to try to rationalise the reaction between arsonium ylides and carbonyl compounds. In the first report of the reaction between a non-stabilised arsonium ylide and a carbonyl compound, they proposed that the reaction commenced as for a normal Witting reaction with nucleophilic attack of the ylide carbanion at the carbonyl carbon atom to form an intermediate betaine. To date, however, no such intermediates have been isolated from reaction mixtures.

More definitive evidence is available for the so-called stabilised arsonium ylides. Johnson[11] has shown that triphenylarsonium fluorenylide distinguishes between aldehydes and ketones as effectively as does its phosphorus analogue[127]. However, in contrast to the latter, the arsonium ylide reacted with all benzaldehydes in nearly equal yields. Furthermore, Johnson only isolated olefins, the normal Wittig products. Accordingly, he proposed the mechanism of reaction to be the same as that for the Wittig reaction with betaine formation as the slow step[10,58].

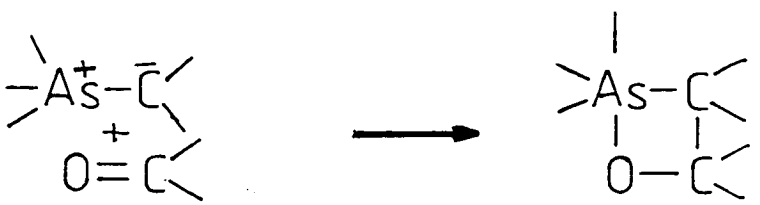
Nesmeyanov and co-workers[128] have measured the rate constants for the reaction of triphenylarsonium phenacylide with several p-substituted benzaldehydes in benzene at 20°C. They found that the reaction was second order (first order in each component) with the rate of aldehyde disappearance equal to the rate of chalcone formation. The reactivity of the aldehydes was found to decrease in the order:

$$Cl > H > CH(CH_3)_2 > OCH_3$$

as might have been expected if the reaction was initiated by nucleophilic attack at the carbonyl carbon. These observations agree with an overall reaction involving a slow, reversible first step (betaine formation) followed by rapid decomposition into products. It is notable that a correlation of the rate data with electron-withdrawing potential of the aldehyde aromatic ring gave a Hammett ρ value of +2.63 which is almost the same as that obtained for the corresponding reaction of triphenylphosphonium carbomethoxymethylide (ρ = 2.7) under similar conditions[129].

In the only other quantitative study to date, Froyen has investigated the kinetics of the reaction of a series of stabilised arsonium ylides with p-nitrobenzaldehyde[21]. The reaction was shown to be second order, first order in ylide and benzaldehyde.

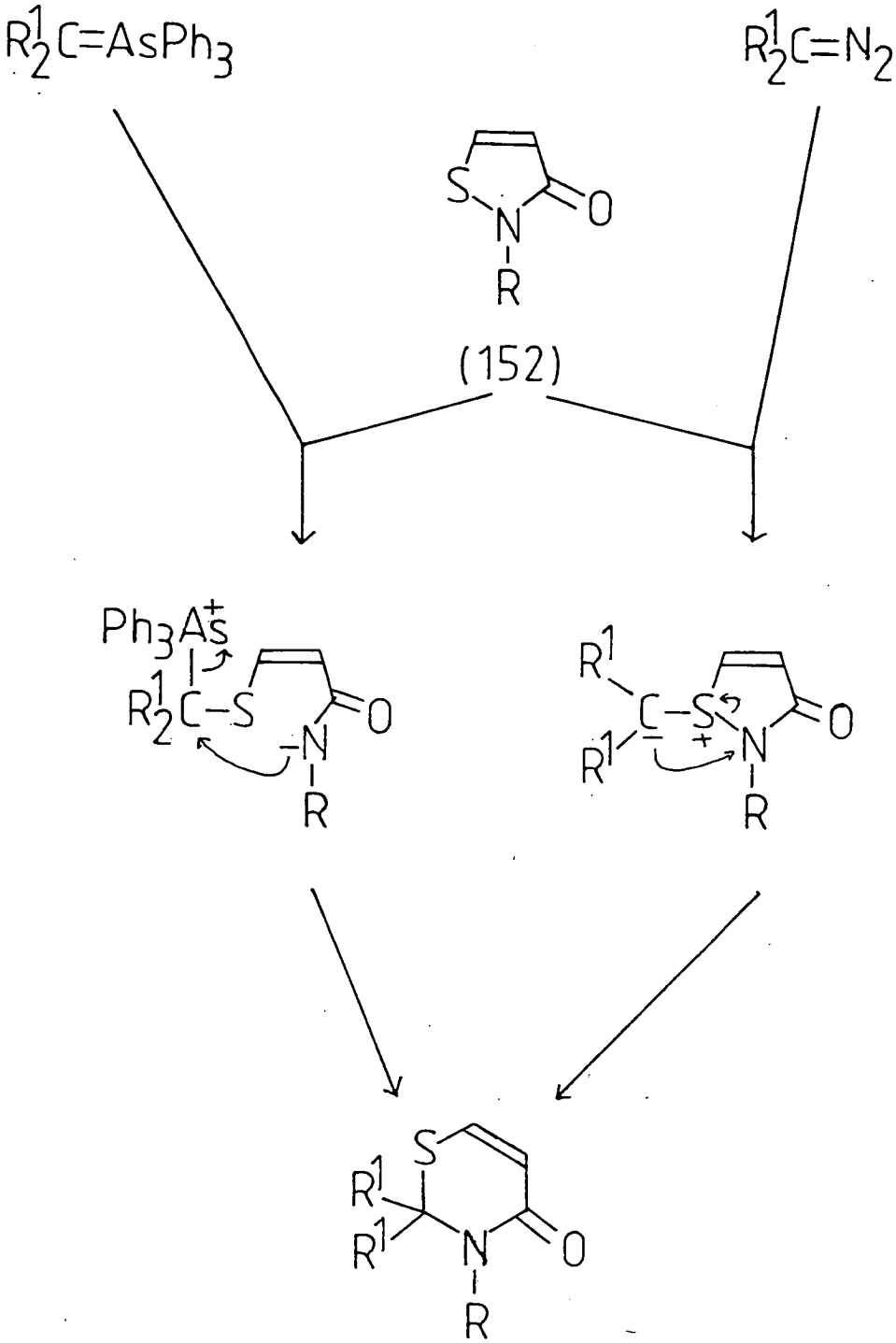
The reaction showed little dependence on the polarity of the solvent, a finding which did not appear to be consistent with the intermediacy of a betaine. This led Froyen to suggest that the reaction proceeded via the neutral four-membered transition state (151), which was formed in one step without the intermediacy of a betaine. This synchronised reaction mechanism is entirely consistent with the very low activation energies observed for the reactions.



(151)

1.5 Programme of Research

The introduction has described the preparation and properties of arsonium ylides, particularly in relationship to their phosphorus and sulphur analogues. Mention has been made of the pioneering work of Gaudiano[13,14,15] who has reported several reactions of arsonium ylides leading to the synthesis of heterocyclic ring systems. The aim of the work undertaken in this thesis was to investigate the utility of arsonium ylides in organic synthesis, especially for the preparation of 1,3-thiazines from 3-isothiazolones (152). The initial approach used to achieve this goal involved nucleophilic attack by arsonium ylides at the



Scheme Fortyseven

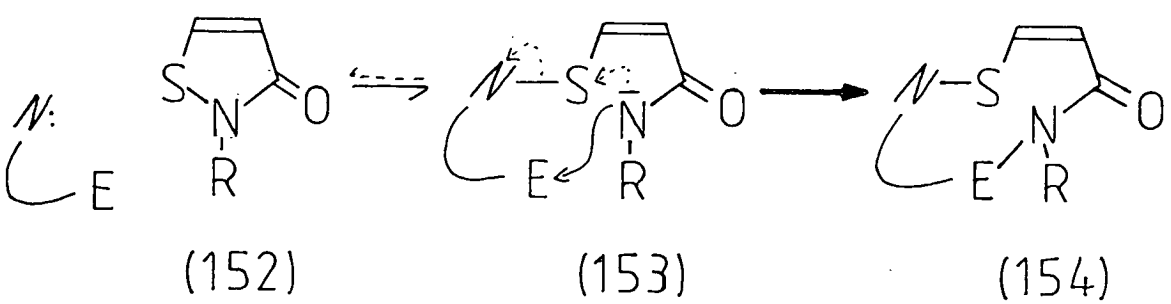
S-N bond as shown in Scheme Fortyseven. This led to a successful approach incorporating electrophilic attack by carbenes at the soft sulphur centre (Scheme Fortyseven).

Two other aspects of arsonium ylide chemistry have also been examined: firstly, reactions with activated olefins and acetylenes, and secondly the effect of solvent on the reaction between arsonium ylides and carbonyl compounds.

2.1 Reaction of arsonium ylides with N-ethyl-3-isothiazolone

2.1.1 Introduction

The possibility of forming heterocyclic systems by utilising the lability of the S-N bond in N-substituted-3-isothiazolones (152) offers considerable scope from a synthetic viewpoint. As depicted in Scheme Fortyeight a reaction sequence can be envisaged involving initial ring-cleavage by nucleophilic attack at the sulphur atom, followed by cyclisation brought about by a suitable electrophilic site in the addendum (i.e. amide nitrogen), e.g. (153) → (154).



(152) (153) (154)

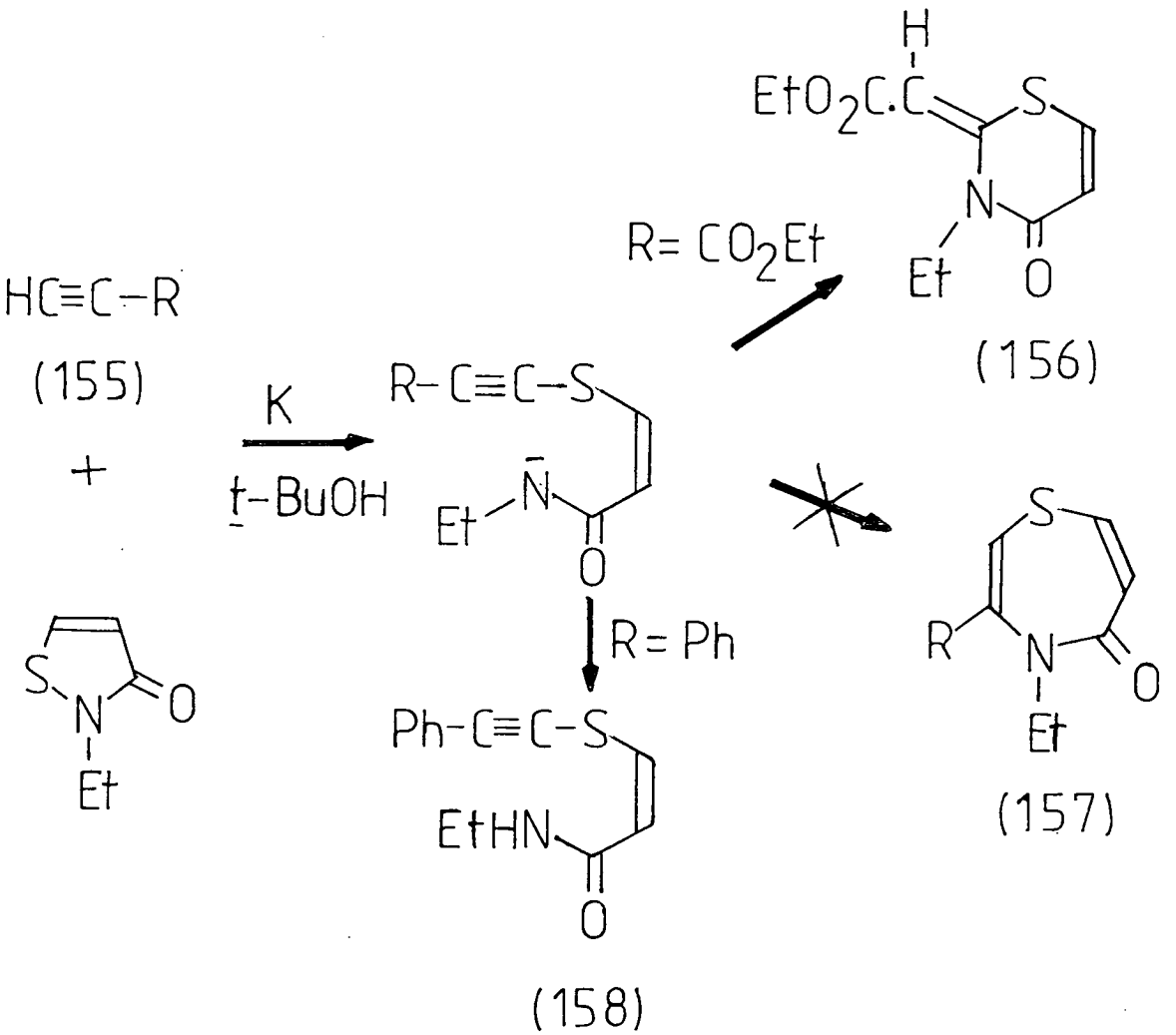
N = nucleophilic site

E = electrophilic site

Scheme Fortyeight

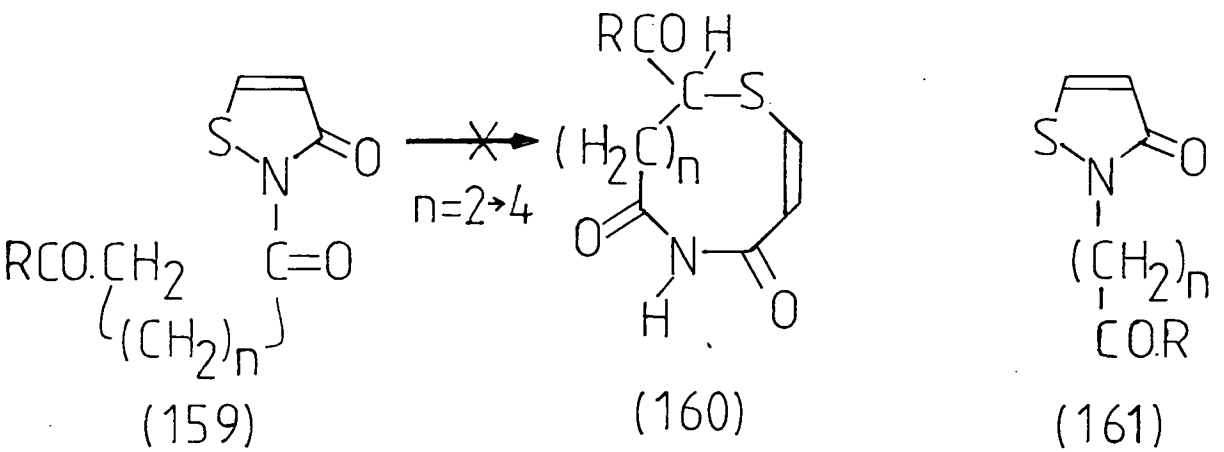
In the only example to date, the base catalysed condensation of ethyl propiolate (155, R = CO_2Et) with N-ethyl-3-isothiazolone (152, R = Et) afforded the 1,3-thiazine (156) in preference to the seven-membered thiazepine (157)[130]. However, the reaction proved not to be general, and in the case of phenylacetylene (155, R = Ph) the open-chain mercaptoacrylamide (158) was formed, apparently because the phenyl group was unable to provide sufficient

stabilisation for the incipient carbanion resulting from Michael attack at the triple bond. A similar reaction with 1-butyne-3-one gave only tarry materials.



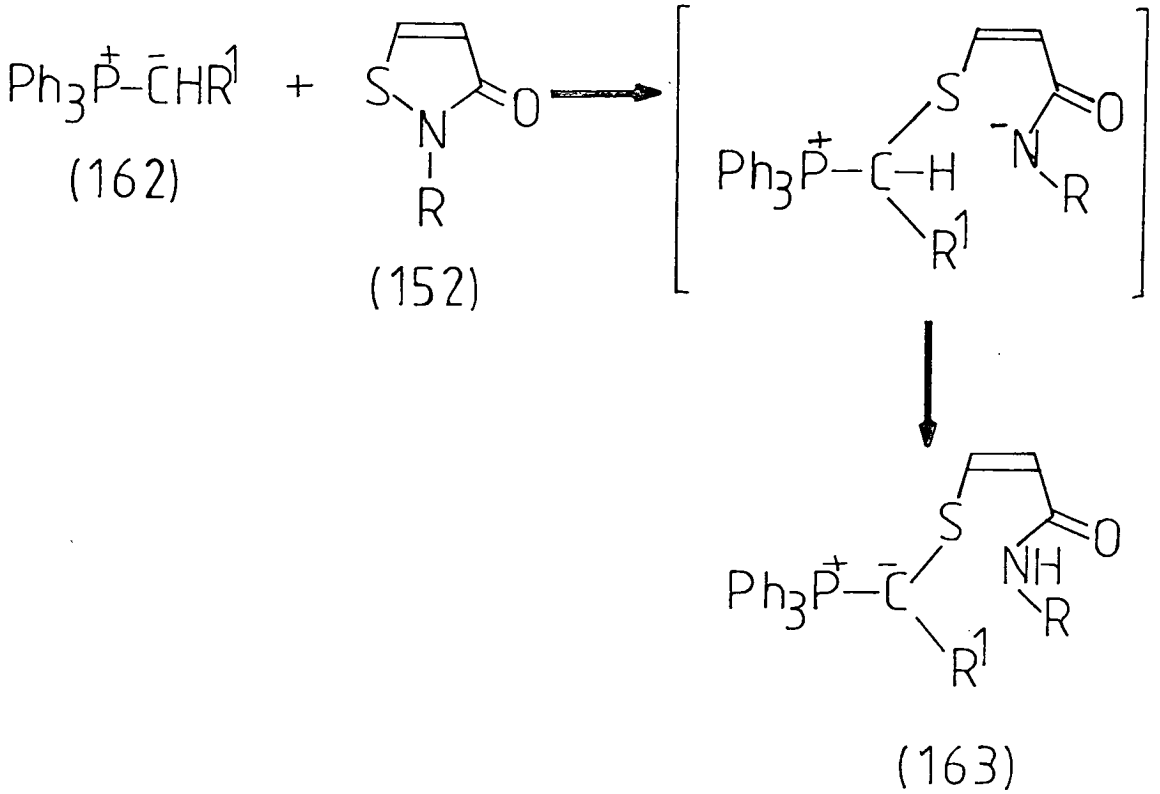
For the reaction sequence shown in Scheme Fortyeight to be effective it must compete with the possible reversal of the initial step, a pathway previously shown to occur by Crow and Gosney with stabilised carbanions[131-133]. Other studies, notably by Chan[134], have shown that attempts to effect an intramolecular attack, e.g. (159) → (160) suffer from either hydrolysis of the N-acyl substituent, or alternatively lead to the polymerisation of the substrate

via the formation of an anion at C-5. Other attempts to generate a carbanion in long chain N-alkyl-3-isothizaolones possessing terminal acyl substituents (161) also failed due to dimerisation, as did reactions in which Grignard reagents were formed in the terminal position of long chain N-alkyl halides.



(159) (160) (161)

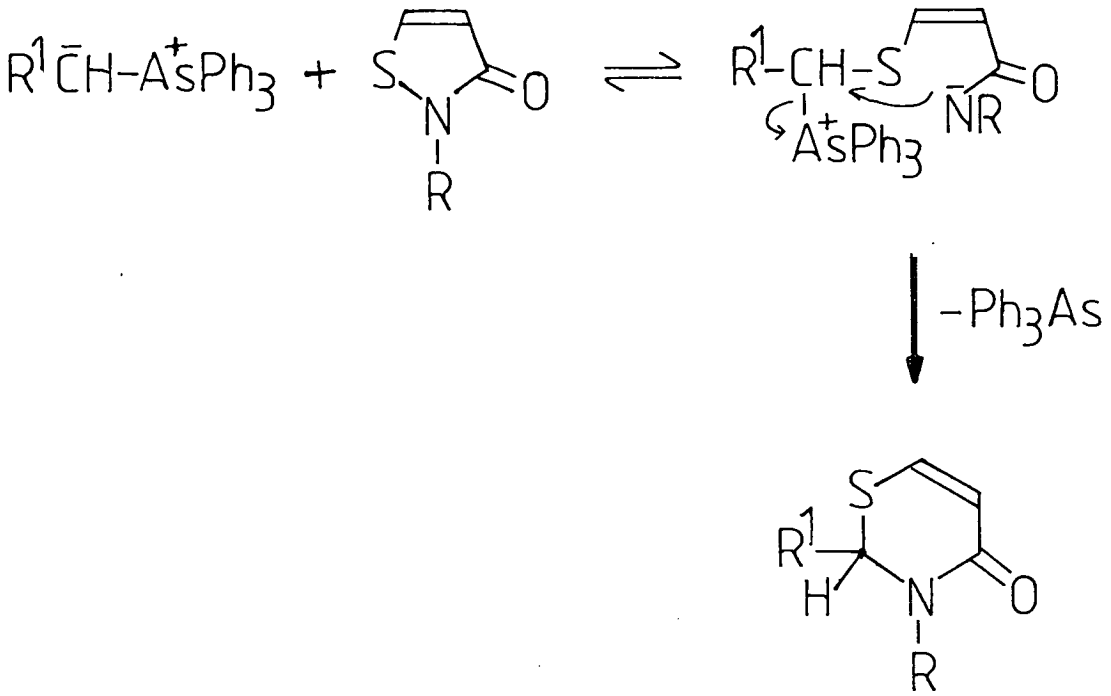
The facile cleavage of the S-N bond in N-substituted-3-isothiazolones by carbanions, as demonstrated by Crow and Gosney[131], pointed to the liklihood of similar reactions with other nucleophiles, especially ylides which can be regarded as modified carbanions. In this connection, Gosney[130] has shown that the phosphonium ylide (162, R^1 = CO_2Me) condensed with N-acyl-3-isothiazolones (152, R = CO_2Et, COMe, CHO) at low temperature in acetonitrile to give the new ylides (163, R^1 = CO_2Me) in high yield, apparently via a prototropic shift (Scheme Fortynine). By contrast, the ylides (162, R^1 = COPh, COMe, CO_2Me) failed to react with N-ethyl-3-isothiazolone in boiling acetonitrile, although ring cleavage did occur with the more labile N-acyl-3-isothiazolones (152, R = CO_2Et, COMe, CHO).



(162) (152) (163)

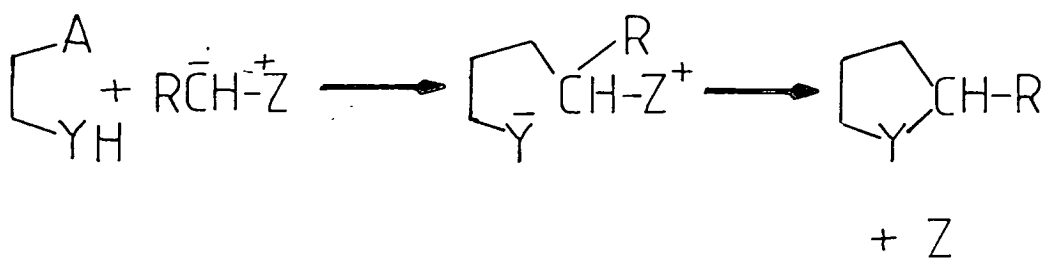
Scheme Fortynine

In view of the greater nucleophilicity of arsonium ylides compared to phosphonium ylides[52] it seemed worthwhile to investigate their reactions with 3-isothiazolones, especially since ejection of the arsine moiety would afford a simple but effective route to 1,3-thiazines (Scheme Fifty). The latter are of considerable interest due to their use as anti-radiation agents and as radiation-sickness drugs[135]. They also display some insecticidal and fungicidal activity[136].



Scheme Fifty

As mentioned in the Introduction, arsonium ylides have already lent themselves to the successful synthesis of several five-membered heterocycles by a similar strategy. In general, this approach involved reaction of the ylides with open-chain compounds according to Scheme Fiftyone.



A - electrophilic centre in substrate

Y - nucleophilic heteroatom (N, O, S)

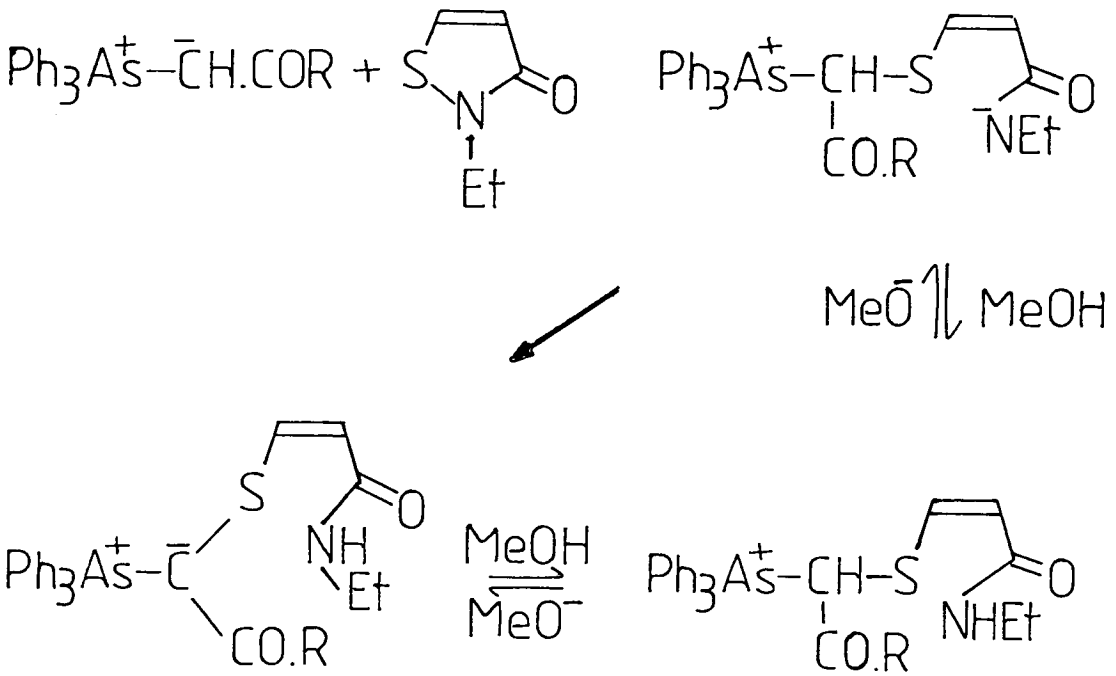
Z^+ - ylidic onium group (sulphonium, arsonium).

Scheme Fiftyone

2.1.2 Reaction with stabilised arsonium ylides

Reaction between N-ethyl-3-isothiazolone and triphenylarsonium carbomethoxymethylide failed to occur in benzene at room temperature. However, when treated with the ylide in methanol at room temperature, N-ethyl-3-isothiazolone underwent rapid ring cleavage to afford, after chromatography over alumina, a colourless crystalline compound (27.6%). Microanalysis indicated that the compound had the empirical formula $C_{26}H_{26}AsNO_3S$ while the mass spectrum exhibited the triphenylarsine fragmentation pattern typical of stabilised triphenylarsonium ylides[40,137]. The presence of a typical NH stretch (3285 cm^{-1}) in the i.r. spectrum indicated that ring cleavage of the N-ethyl-3-isothiazolone had occurred followed by protonation of the amide anion, presumably by a prototropic shift. The ^1H n.m.r. spectrum of the compound confirmed that it was a ring opened product as demonstrated by the cis-olefinic coupling of 10.6 Hz between the two methine protons at δ6.53 and 5.51. The combined analytical and spectroscopic evidence suggested that the compound had the structure (164). Further experiments showed that the stabilised ylide (164) could be prepared (22%) in the absence of solvent by heating the reactants in a melt at 70°C.

In a further experiment, the stabilised ylide (165) was formed by reaction of triphenylarsonium phenacylide with N-ethyl-3-isothiazolone in methanol. Again, the ylide was purified by chromatography over alumina.

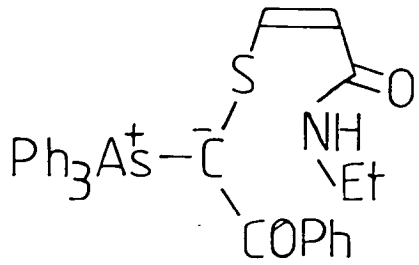


164 : R = OMe

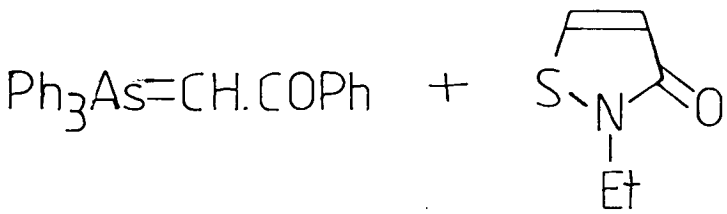
165 : R = Ph

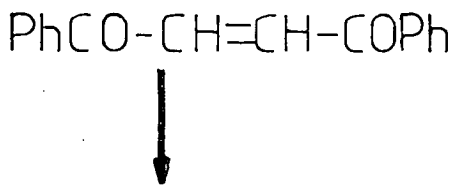
The formation of these new ylides is reminiscent of the reactions involving secondary carbanions with N-ethyl-3-isothiazolones in aprotic solvents[131], whereby initial cleavage of the S-N bond is followed by proton migration via an intramolecular process. In this instance, proton migration to give a highly stabilised ylide is facilitated by the presence of the activating group Ph_3As^+ adjacent to the carbanionic centre. The stability of the derived ylides towards hydrolysis on alumina chromatography columns can be attributed to the stabilising effect of the carbonyl and mercaptoacrylamide moieties attached to the carbanionic centre.

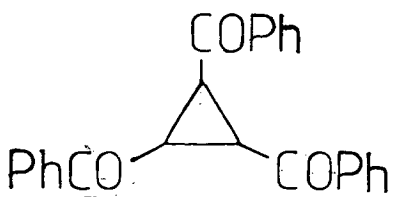
In an attempt to bring about thiazine formation, (165) was boiled in anhydrous toluene for 14 hr, but



(165)





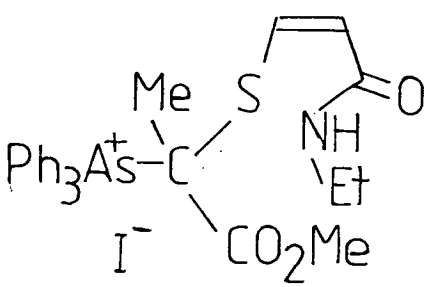


(71)

Scheme Fiftytwo

thermal decomposition ensued to give triphenylarsine (43.8%), triphenylarsine oxide (39.4%), N-ethyl-3-isothiazolone (∿60%), and the cyclopropane (71) (67.4%). A plausible mechanism for the formation of the latter is shown in Scheme Fiftytwo. Apparently, under these conditions thermolysis brings about ring closure, but to a five membered ring, not a six membered ring. In the same way, bulb to bulb distillation (100°C; 0.2 mmHg) of (164) for 30 hr afforded only triphenylarsine and N-ethyl-3-isothiazolone. When boiled in anhydrous benzene for 28 hr, (164) was recovered largely unchanged.

Attempts to oxidise and reduce (164) were also unsuccessful due to fragmentation of the ylide to give N-ethyl-3-isothiazolone. In addition, methylation of (164) with methyl iodide in a sealed tube at 92°C for 20 hr failed to yield the arsonium salt (166). Instead, the ylide decomposed *via* N-ethyl-3-isothiazolone extrusion.



(166)

Similar transylidation reactions have already been discussed in the Introduction.

2.1.3 Reaction with semi-stabilised arsonium ylides

Treatment of triphenylarsonium benzylide, generated by the action of sodium methoxide on its hydrobromide, in the

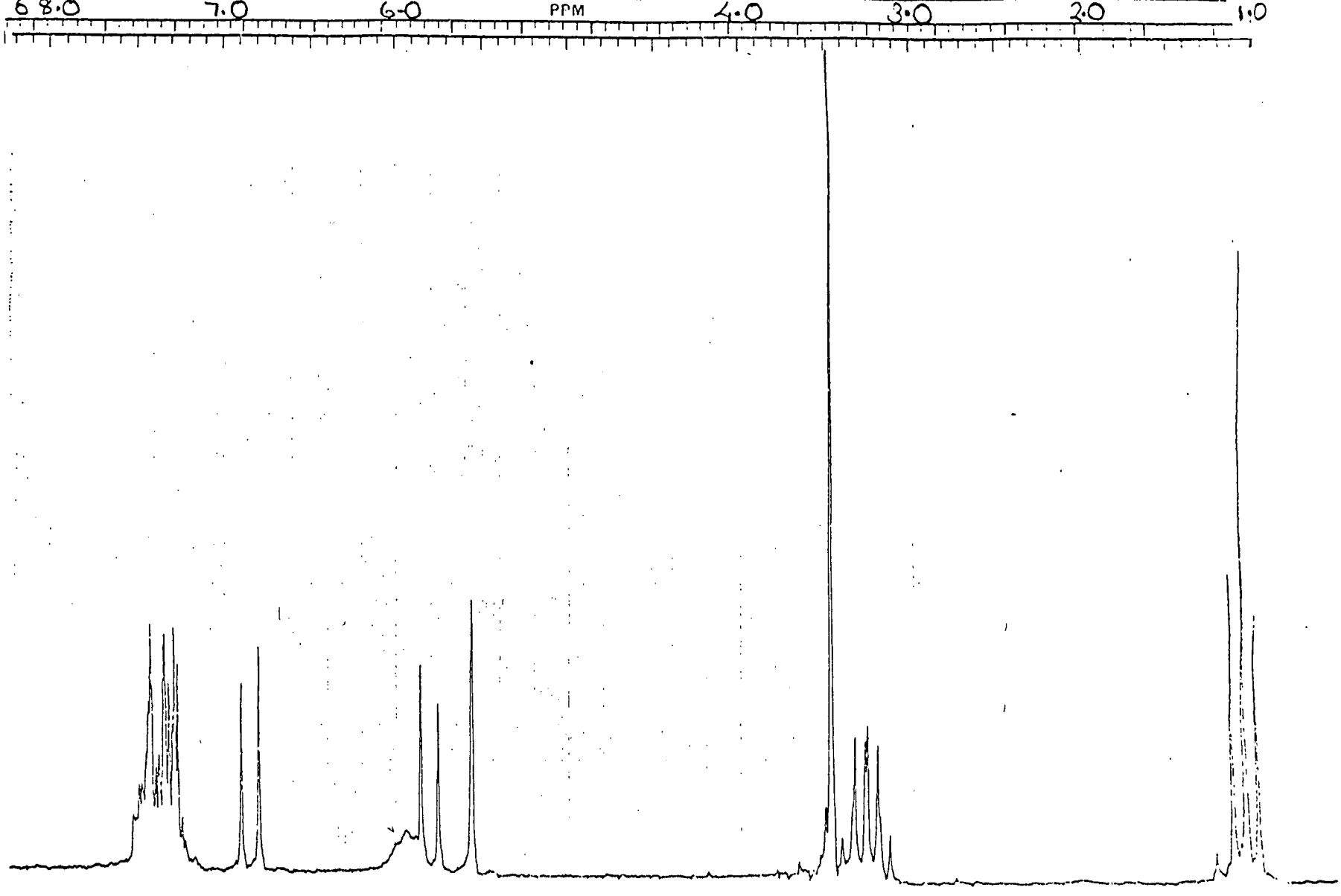


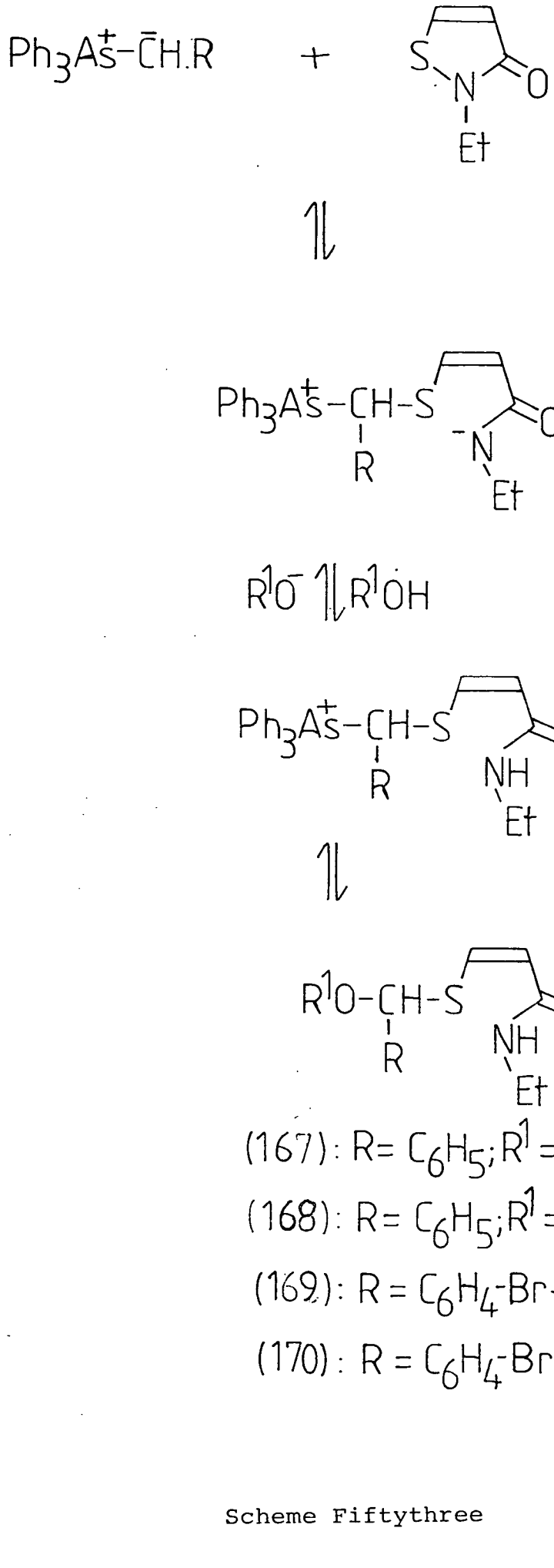
Figure 1. 100 MHz ^{1}H n.m.r. spectrum of (167).

presence of N-ethyl-3-isothiazolone in methanol at room temperature produced a colourless product in high yield together with triphenylarsine. Both products were isolated by column chromatography from alumina.

On the basis of analytical and spectral evidence the structure of the colourless product was established as N-ethyl-cis-3-(α-methoxybenzyl)mercaptoacrylamide (167). (Scheme Fiftythree). Elemental analysis gave percentage compositions for carbon, hydrogen and nitrogen consistent with an empirical formula $C_{13}H_{17}NO_2S$. This was verified by observation in the mass spectrum of a parent ion peak at m/e 251.

The ^1H n.m.r. spectrum of the product is shown in Figure 1. The structurally significant peaks are located at δH 5.94, a broad one proton singlet assigned to a NHEt group, one proton doublets (J = 10.1 Hz) at δ6.85 and 5.80 corresponding to cis-olefinic protons, and δ3.28, a two proton multiplet reduced to a quartet (J = 7.25 Hz) with loss of the signal at δ5.94 upon a D_2O shake; this signal was assigned to a $NHCH_2$ group. Evidence in support of this assignment was obtained from the i.r. spectrum which showed a strong sharp NH stretch at 3280 cm^{-1}.

All previous work has shown that carbanion attack on N-ethyl-3-isothiazolone occurs to give the cis product[131]. In order to unambiguously assign a cis structure to the products obtained from carbanion attack on N-ethyl-3-isothiazolone, Gosney[130] prepared both cis and trans isomers of N-ethyl-3-methylmercaptoacrylamide (as shown in Scheme Fiftyfour), thus allowing comparison of the coupling



(167): R= C_6H_5; R^1 = Me

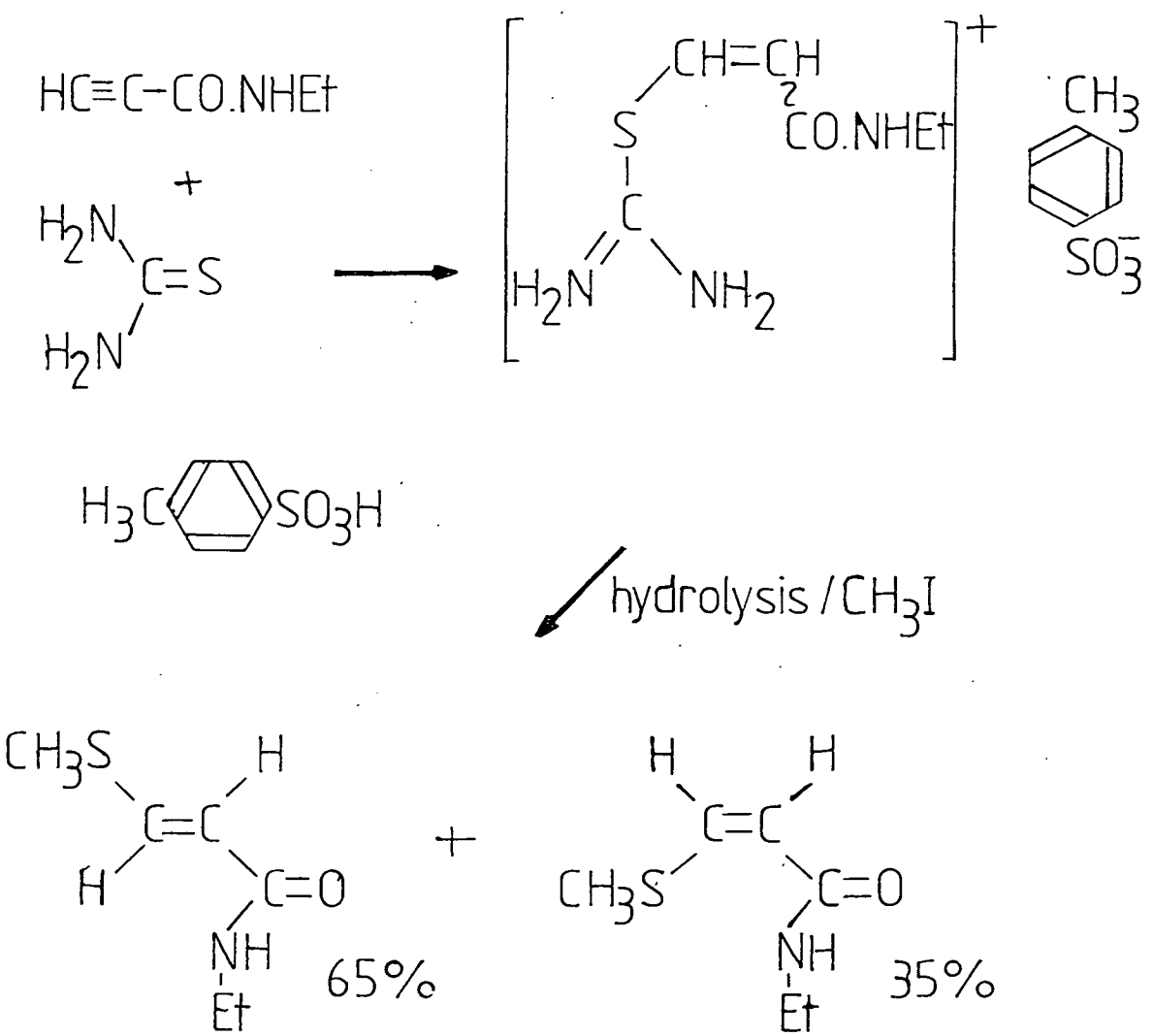
(168): R= C_6H_5; R^1 = Et

(169): R = C_6H_4-Br-p; R^1=Me

(170): R = C_6H_4-Br-p; R^1=Et

Scheme Fiftythree

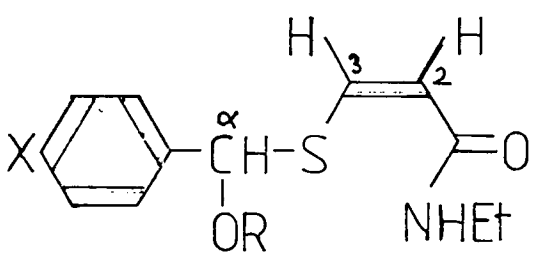
constants. The two isomers of N-ethyl-3-methylmercapto-acrylamide were found not to isomerise under mild conditions. The observed coupling constants of the two isomers (J_{cis} 10.0 Hz and J_{trans} 15.1 Hz) verified the cis conformation of the products from ring scission and nucleophilic addition. The coupling constant (J = 10.1 Hz) observed for the monothioacetal (168) agrees with the previously reported coupling constants for cis-N-alkyl-mercaptoacrylamides[131]. Indeed, all products reported in this thesis from ring scission are cis isomers and post-isomerisation did not occur in any case.



Scheme Fiftyfour

Similar reactions with other ylides yielded the corresponding ring-opened products. Thus, reaction with triphenylarsonium benzylide in ethanol gave N-ethyl-cis-3-(α-ethoxybenzyl)mercaptoacrylamide (168), while reaction with triphenylarsonium p-bromobenzylide gave N-ethyl-cis-3-[α-methoxy(p-bromobenzyl)]mercaptoacrylamide (169) in methanol, and N-ethyl-cis-3-[α-ethoxy(p-bromobenzyl)]-mercaptoacrylamide (170) in ethanol.

A possible mechanism for the formation of the monothioacetals is delineated in Scheme Fiftythree. It appears that solvolysis of the initial 1:1 adducts is the favoured pathway, rather than arsine extrusion by an amide nitrogen leading to thiazine formation.



(171)

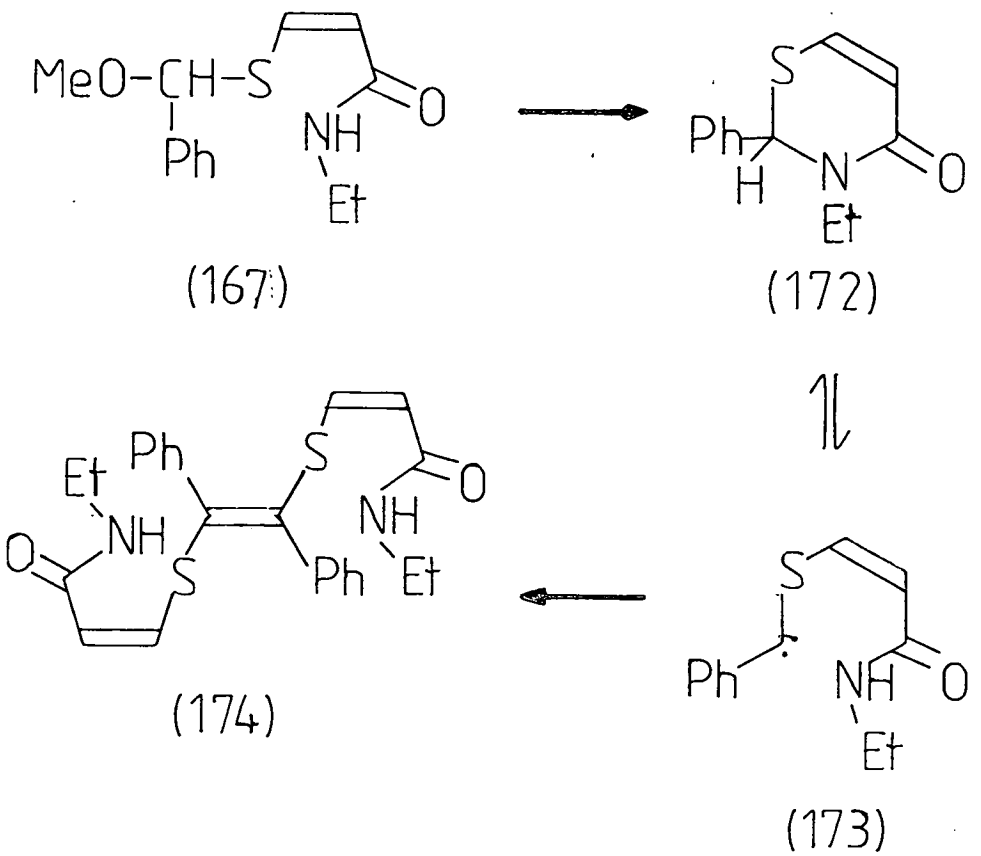
$\delta(CDCl_3)$; p.p.m.

R	X	NH	H2	H3	Hα
H^{131}	H	6.3	5.81	6.73	3.87
OMe	H	5.94	5.80	6.85	5.56
OMe	Br	6.2-6.0	5.82	6.74	5.49
OEt	H	6.26	5.81	6.83	5.6
OEt	Br	6.3-6.1	5.85	6.77	5.59
H	NO_2	5.6	5.75	6.70	3.94

Table 6 Summary of n.m.r. assignments for the mercaptoacrylamides (171).

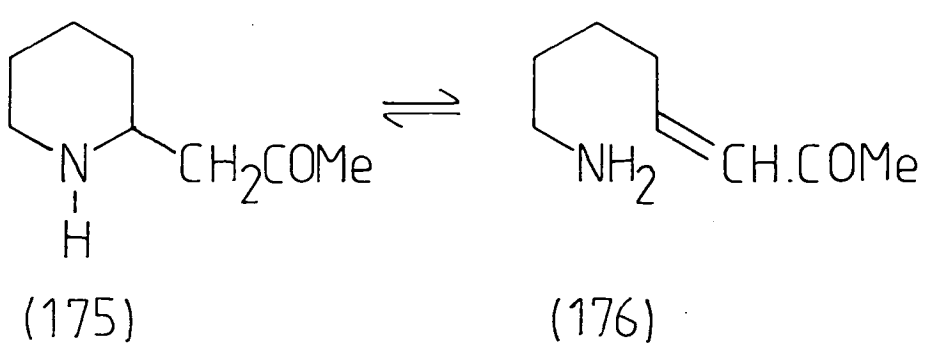
Comparison of the ^1H n.m.r. parameters of the monothioacetals with those obtained by Crow and Gosney[131] for mercaptoacrylamides makes it possible to assign chemical shifts to the methine protons of the monothioacetals. Thus, the downfield doublet can be attributed to the methine proton adjacent to the sulphur, while the upfield doublet is due to the methine proton adjacent to the amide (Table 6). Presumably the low field methine proton reflects the acidity afforded to protons by an α-sulphur atom[138]. This is often ascribed to sulphur valence shell expansion although no conclusive proof for this explanation has been advanced[139].

All attempts to convert the monothioacetal (167) into the 1,3-thiazine (172) failed. Thus, when pyrolysed under flash vapour conditions at 140°C/0.001 mmHg the monothioacetal was recovered unchanged, although thermolysis in a Kugelrohr oven at 150°C/2mmHg did yield a white gum (41%). Its i.r. spectrum exhibited absorptions at 3330 (NH) and 1630 (C=O) cm^{-1}. An accurate mass determination for the small parent ion peak at m/e 438 in the mass spectrum suggested a molecular formula of $C_{24}H_{26}N_2O_2S_2$ which implied that the product was the result of an intermolecular reaction. Significantly, the ^1H n.m.r. spectrum of the product showed a lack of methoxy resonances. A possible structure which satisfies the loss of methanol and the other spectroscopic data is (174), but the mechanism for its formation remains unclear. It is feasible that initial nucleophilic attack by the amide nitrogen did occur to give the 1,3-thiazine but subsequent dimerisation via its carbene tautomer (173) occurred (Scheme Fiftyfive).

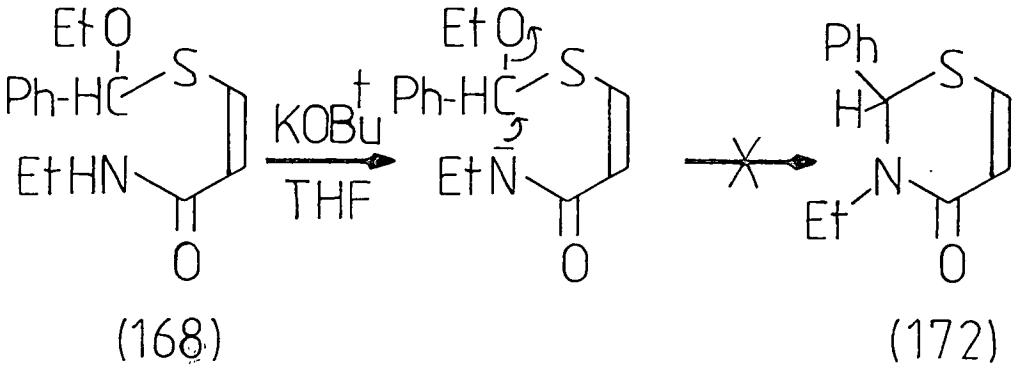


Scheme Fiftyfive

A similar example of ring-chain tautomerism is found in the ready racemisation of isopelletierine (175) via the open-chain form (176)[140]. Tautomerism of this type is also observed with meso-ionic compounds[141]. Thus, while the evidence points towards the dimer structure, further work is necessary to confirm the proposed structure. However, it seems unlikely that the monothioacetal would undergo loss of methanol on thermolysis to give the carbene (173).



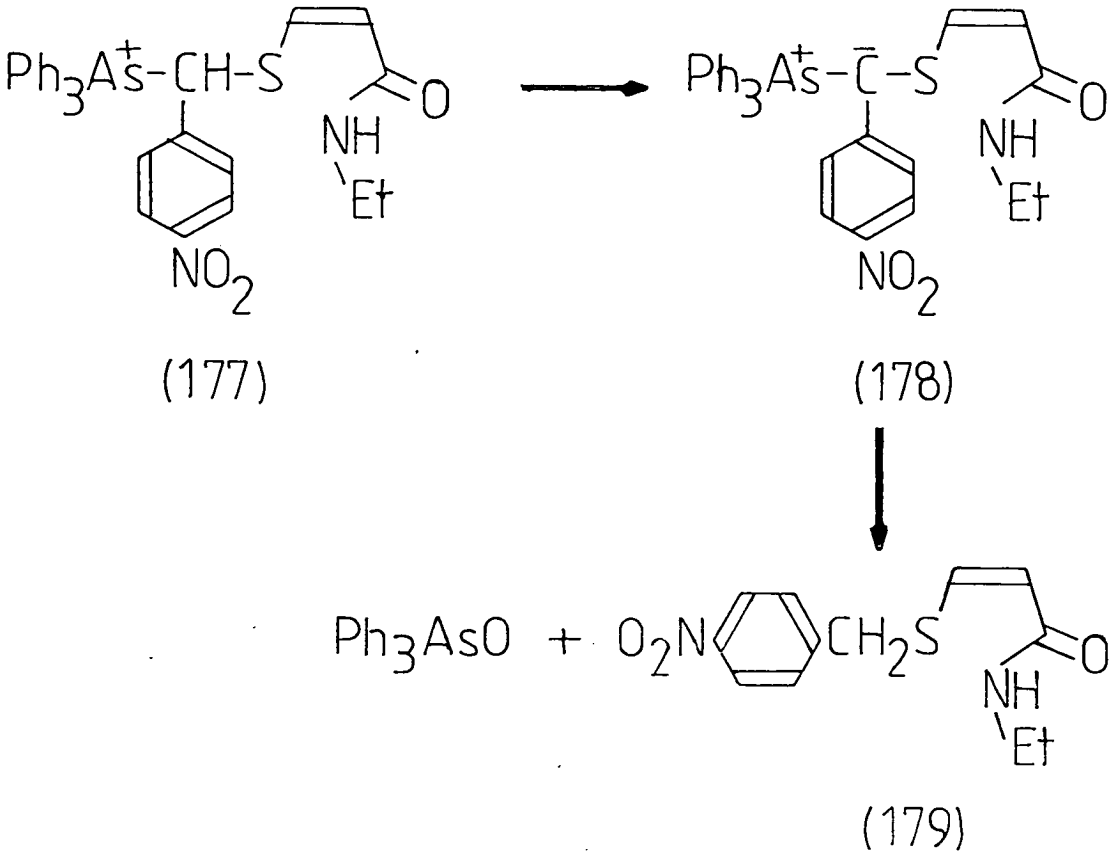
An attempt to cyclise the monothioacetal (168) in tetrahydrofuran at 60°C using potassium tert-butoxide also proved unsuccessful (Scheme Fiftysix).



(168) (172)

Scheme Fiftysix

The corresponding reaction of N-ethyl-3-isothiazolone with triphenylarsonium p-nitrobenzylide also led to ring-cleavage but in this instance a prototropic shift in the initial 1:1 adduct (177) rather than expulsion of triphenylarsine from the initial adduct apparently occurred. Thus, as with stabilised arsonium ylides, a further stabilised arsonium ylide is produced. However, attempts to isolate the resultant ylide (178) were unsuccessful, and only hydrolysis products, triphenylarsine oxide and N-ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide (179) could be obtained (Scheme Fiftyseven).

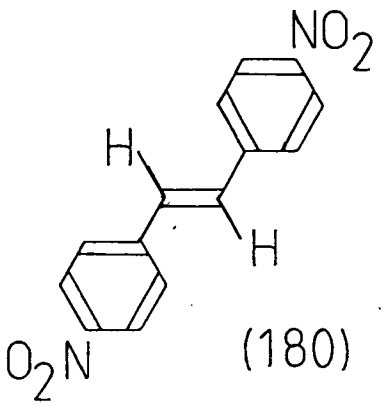


(177) (178) (179)

Scheme Fiftyseven

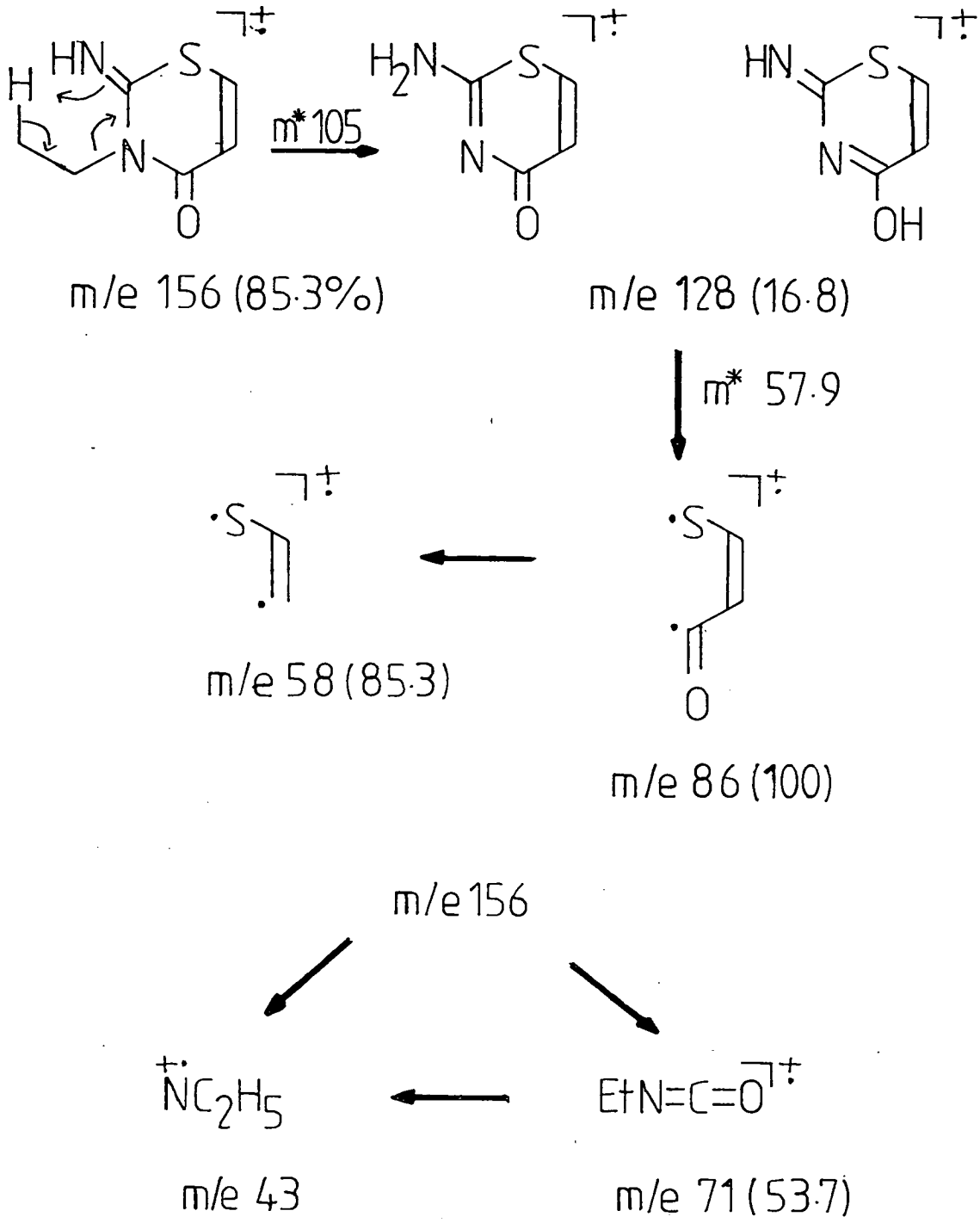
All of the products obtained from the fore-going reactions of semi-stabilised ylides with N-ethyl-3-isothiazolone in an alcoholic solvent can be looked upon as arising by solvolysis. In an attempt to circumvent this problem, and promote thiazine formation, the reactions were repeated in tetrahydrofuran solution by generating the ylide in situ from its hydrobromide salt with either n-butyllithium or sodium hydride. In the reaction with triphenylarsonium benzylide, triphenylarsine was again obtained, but the desired 1,3-thiazine (172) was not found. The only other product isolated after chromatographic work-up of the reaction mixture showed a peak at m/e 159 in its mass spectrum. This compound also exhibited an absorption at 1630 cm^{-1} but the scant information available does not allow its identification.

Triphenylarsonium p-nitrobenzylide did not react with N-ethyl-3-isothiazolone in tetrahydrofuran to give any isolable isothiazolone derivatives. Upon chromatography of the reaction mixture N-ethyl-3-isothiazolone was recovered together with triphenylarsine and stilbene (180). Presumably, the latter was formed by thermal decomposition of the ylide, as described in the introduction (see p.39).

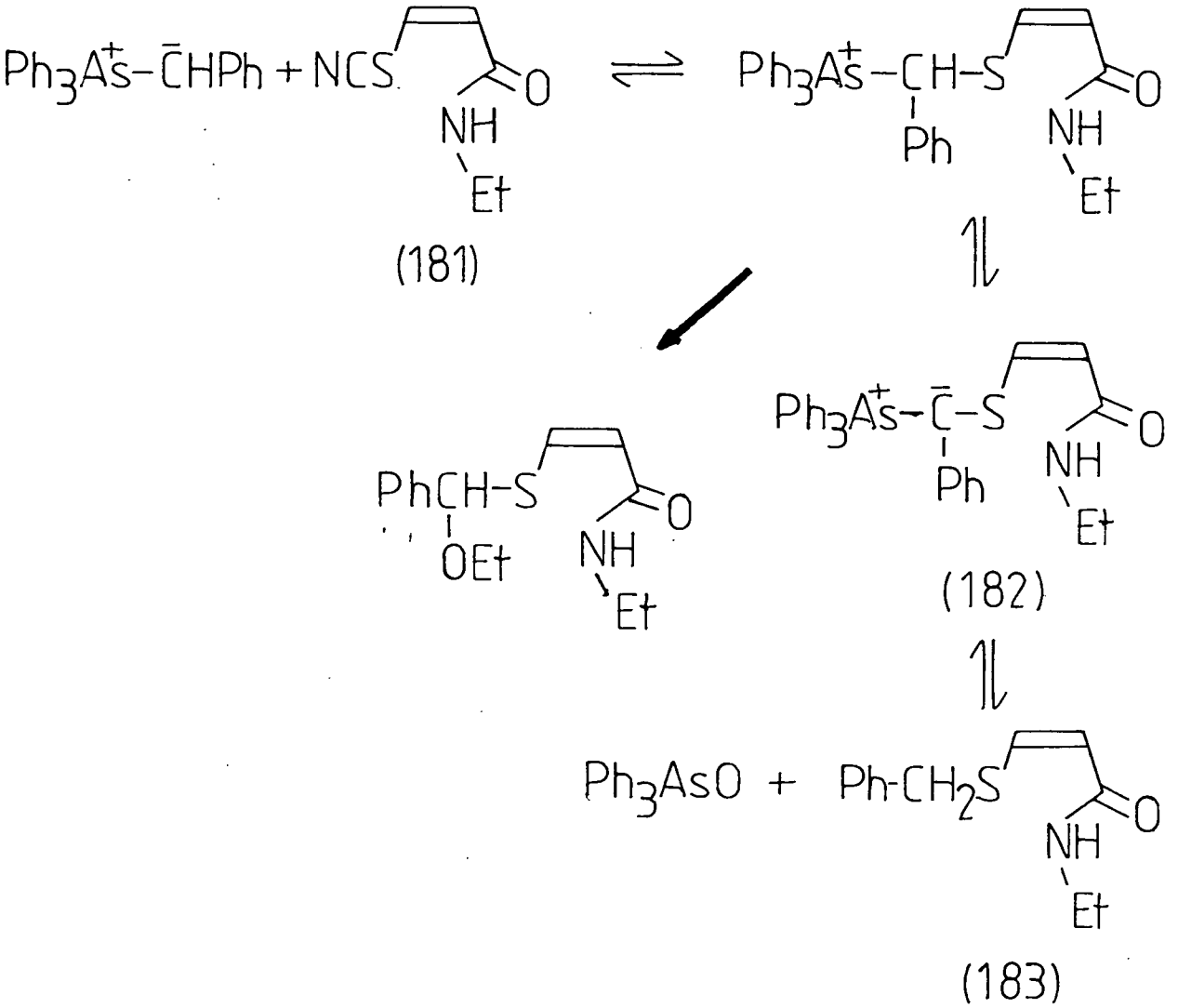


(180)

Reaction of cis-N-ethyl-3-thiocyanoacrylamide (181) might be expected to react with arsonium ylides in the same way that N-ethyl-3-isothiazolone does, hence a brief comparative study was conducted. Thus, two related experiments were carried out in ethanol between the ylides, triphenylarsonium benzylide and p-nitrobenzylide, and the thiocyanoacrylamide (181). In the first, reaction with triphenylarsonium benzylide afforded three isolated products upon chromatography, namely triphenylarsine, N-ethyl-cis-3-benzylmercaptoacrylamide (183), which was thought to be formed by the hydrolysis of ylide (182) (Scheme Fiftyeight).



Scheme Fiftynine.



Scheme Fiftyeight

In the other experiment, reaction with triphenylarsonium p-nitrobenzylide gave four isolated products, triphenylarsine, N-ethyl-cis-3-ethylmercaptoacrylamide (184), N-ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide (179) and a colourless compound which, on the basis of analytical and spectral evidence, was established as 2-imino-3-ethyl-4-oxo-2,3-dihydro-1,3-4H-thiazine (185). The latter is an isomer of the starting thiocyanoacrylamide (181). Elemental analysis gave percentage compositions for carbon, hydrogen and nitrogen consistent with an empirical formula $C_6H_8N_2OS$. This was verified by observation in the mass spectrum of a

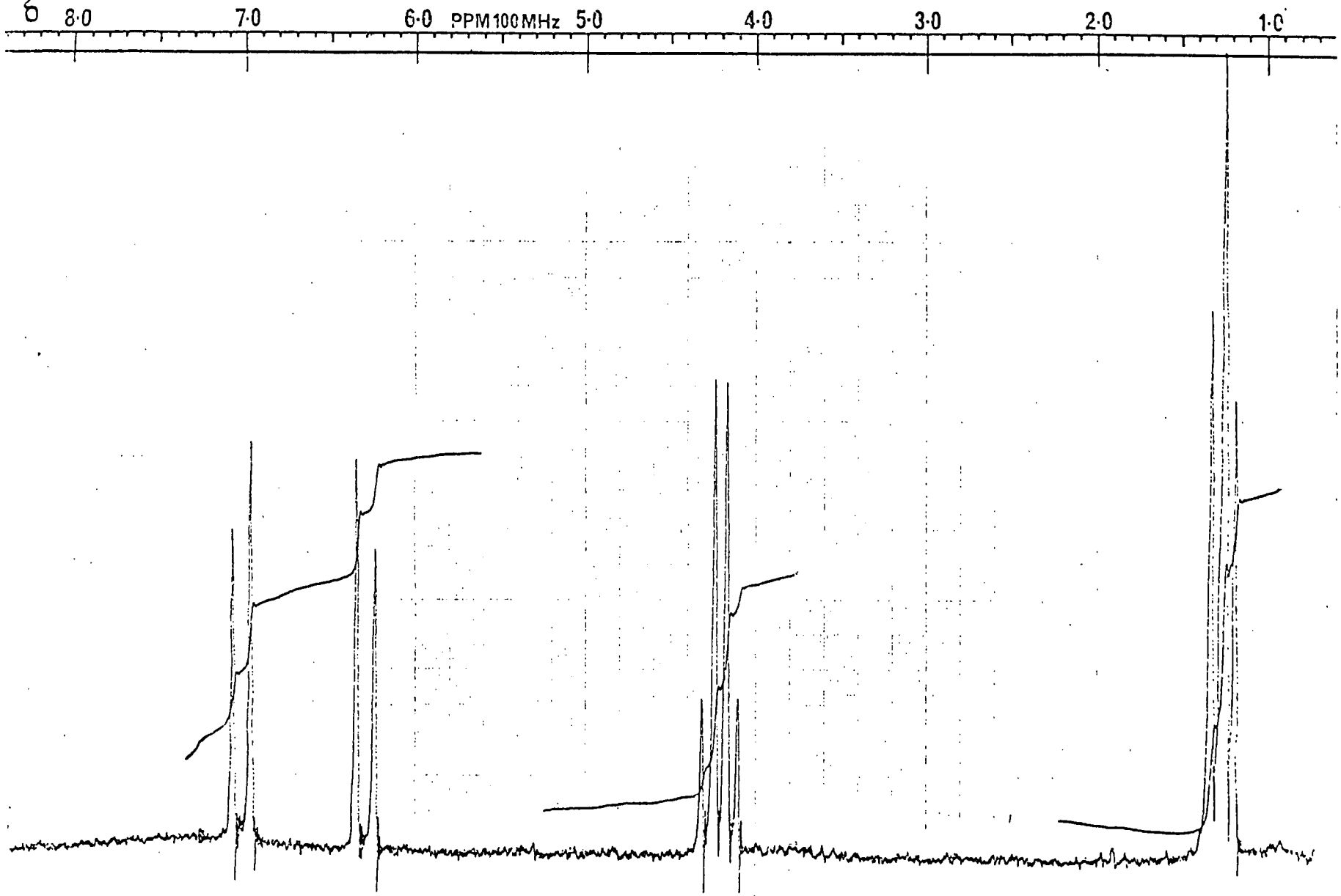
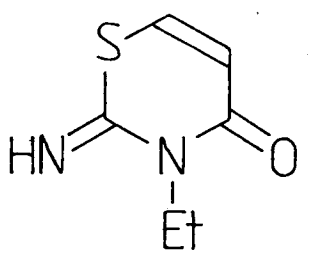


Figure 2. 100 MHz ^{1}H n.m.r. spectrum of (185).

parent ion peak at m/e 156. The ^{1}H n.m.r. spectrum of the thiazine (Figure 2) showed a broad amino proton singlet of one proton at δ8.0-7.5 and two single protons as doublets (J = 10.4 Hz) at δ6.99 and 6.28 (c.f. the 1,3-thiazine (156) obtained by Gosney[130] which exhibited a $J_{\underline{cis}}$ = 10.5 Hz). The i.r. spectrum of the product showed an NH stretching frequency at 3285 cm^{-1} and a carbonyl stretching frequency at 1655 cm^{-1}, but no cyano stretching frequency. This spectral data is consistent with the 1,3-thiazine structure (185) which also fits the mass spectral fragmentation pattern as shown in Scheme Fiftynine.

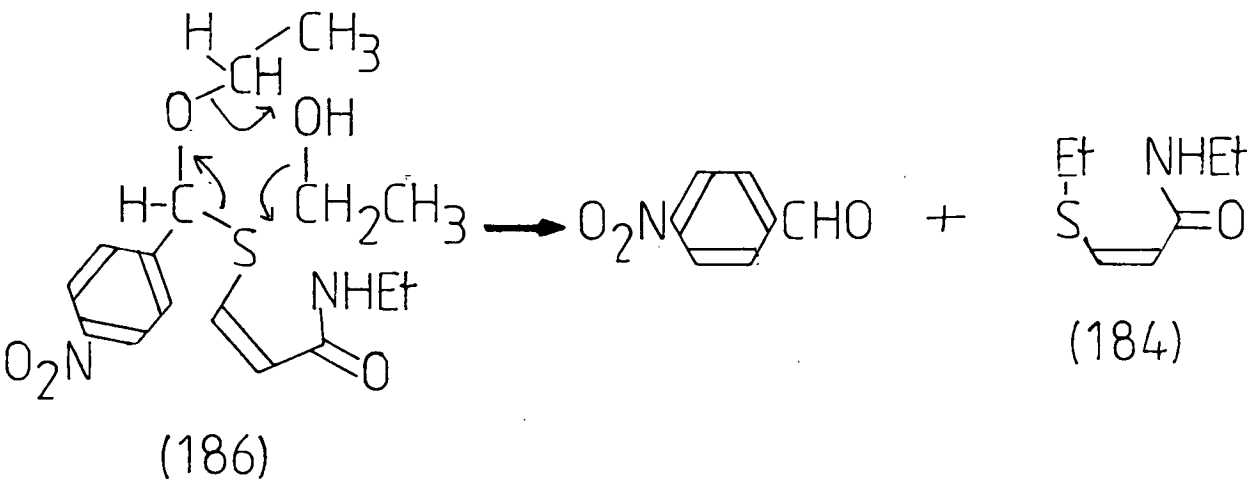
(181) ⟶ 

(185)

No attempt was made to elucidate the mechanism or the reaction conditions required for optimisation of the thiazine yield. However, subsequent experiments confirmed that the isomerisation of (181)→(185) was not a thermal rearrangement. Thus, the thiocyanoacrylamide sublimed at 100°C/1.0 mmHg without rearrangement, whilst more vigorous heating prior to sublimation afforded N-ethyl-3-isothiazolone in high yield. In view of these results, it is not unreasonable to assume that the isomerisation is base-catalysed.

With regard to the mercaptoacrylamide (183), it is presumably formed in the same way as (179), whilst the

generation of (184) can be explained by the decomposition of the monothioacetal (186) as shown in Scheme Sixty. This observation may account for the failure to obtain the thioacetal (186), at least in this case, although no p-nitrobenzaldehyde or stilbene (180) could be detected in the reaction mixture.

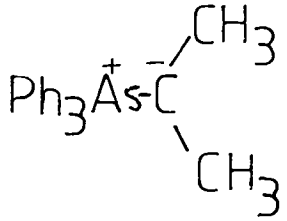


Scheme Sixty

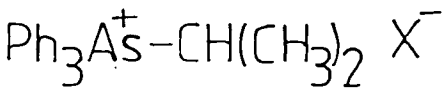
2.1.4 Reaction with reactive arsonium ylides

In order to remove the possibility of proton migration leading to secondary ylide formation, it was decided to utilize triphenylarsonium isopropylide (187) as a reactant. Some difficulty was experienced in preparing a suitable precursor salt since triphenylarsine failed to react with 2-bromopropane under the normal conditions for salt preparation by the action of an arsine on an alkyl halide. This is sometimes unsuccessful due to the presence of a sterically hindered reaction centre or involvement of an arsine that is insufficiently nucleophilic, leading to an unfavourable equilibrium.

Under normal conditions triphenylarsine failed to react with 2-iodopropane, but reaction in a sealed tube (100°C; 66 hr) afforded a poor yield of isopropyltriphenylarsonium triiodide (188) (7.7%). As expected, this salt was decolourised by sodium thiosulphate solution.



(187)

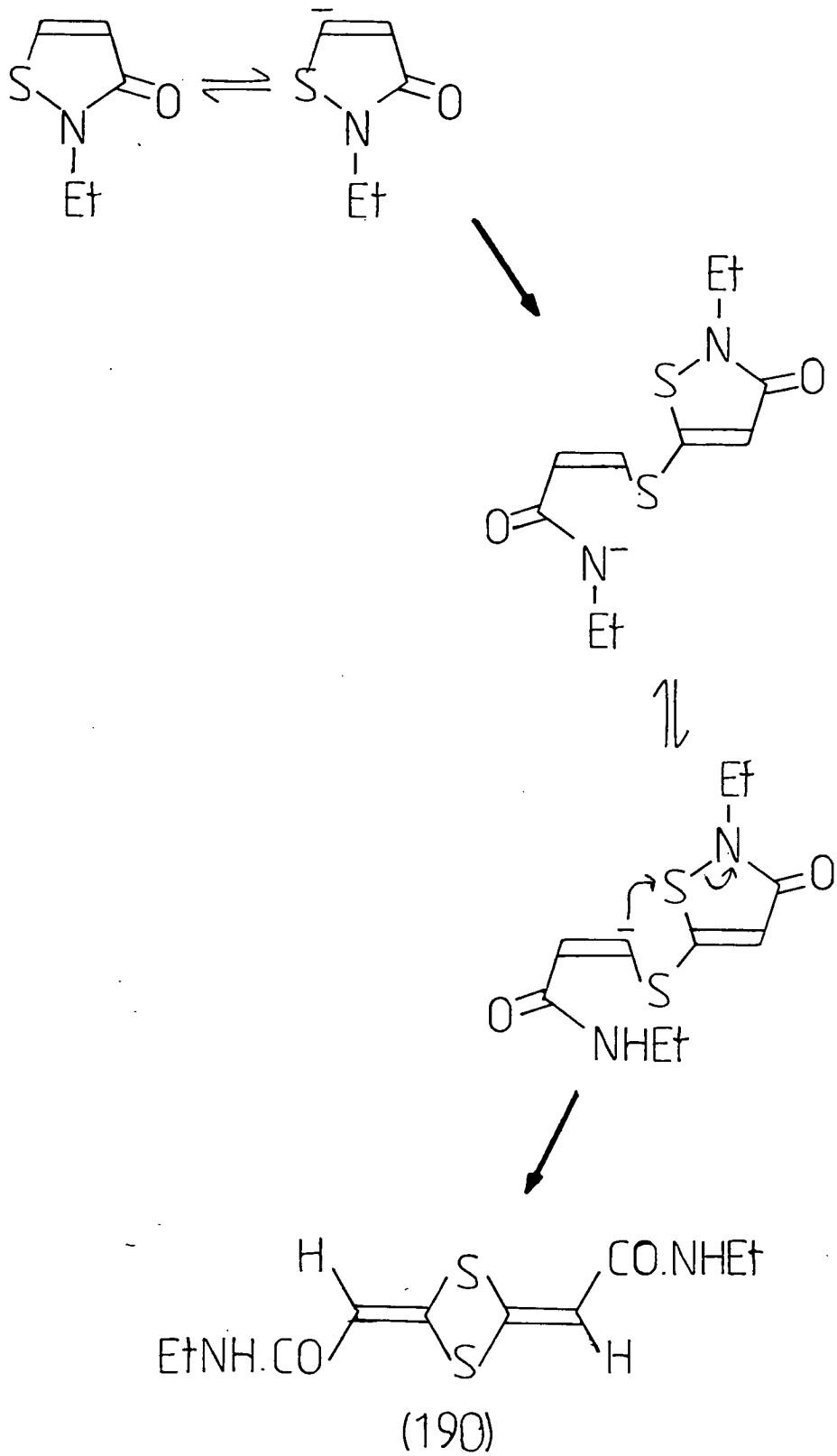


(188): X = I_3

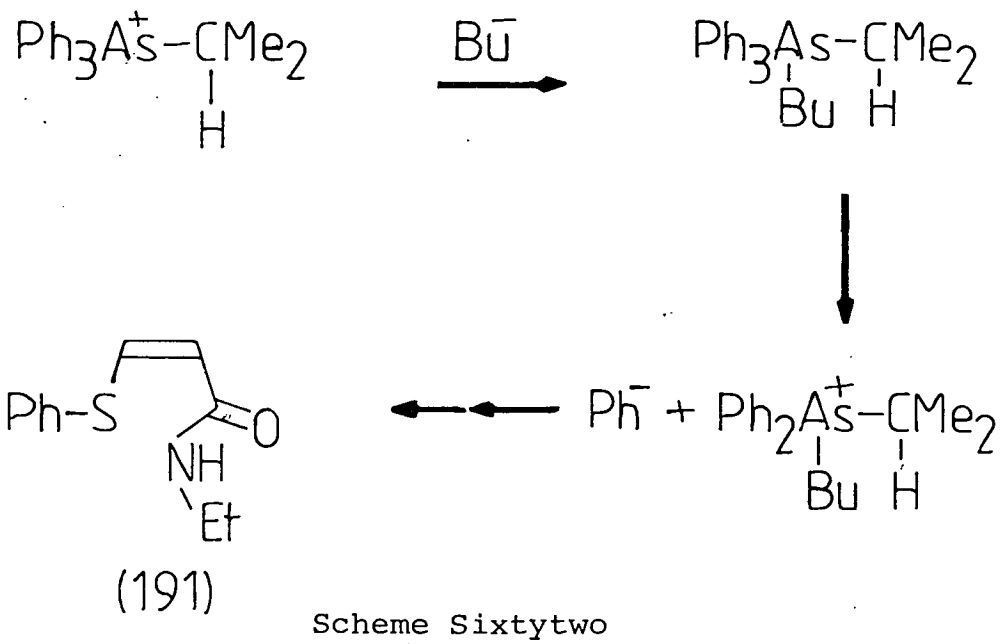
(189): X = BF_4

The desired arsonium salt (189) was eventually prepared by the method of Dwyer[142], whereby a solution containing triphenylarsine and 2-bromopropane was treated with silver tetrafluoroborate in the dark and stirred for 24 hr.

The ylide (187) was generated by treatment of isopropyltriphenylarsonium tetrafluoroborate with butyllithium in tetrahydrofuran at -50°C and N-ethyl-3-isothiazolone added dropwise to the yellow solution. Evaporation of the reaction mixture after 5 hr afforded an oil which was triturated with dichloromethane to give a colourless compound identified as the isothiazolone dimer, 2,4-bis(N-ethylcarboxamido)methylene-1,3-dithietane (190) Chromatography of the leachings from alumina afforded only triphenylarsine, N-ethyl-cis-3-phenylmercaptoacrylamide (191) and triphenylarsine oxide.



Scheme Sixtyone



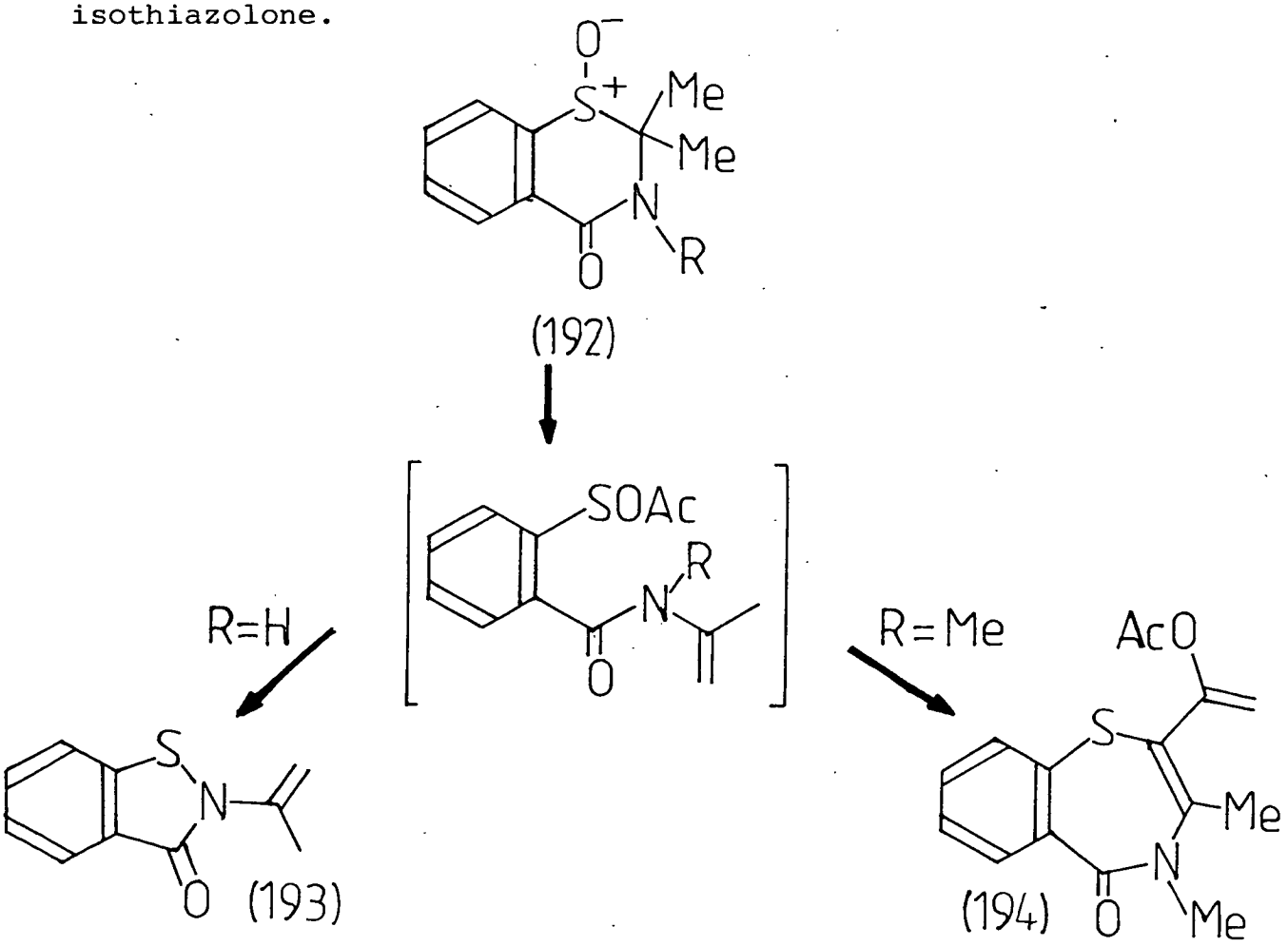
Scheme Sixtytwo

With the exception of the formation of the mercaptoacrylamide, these results accord well with those for the reaction of N-ethyl-3-isothiazolone with tertiary carbanions[133,143] in which the dimer (190) is formed by the mechanism of Scheme Sixtyone. A plausible explanation for the unexpected formation of the mercaptoacrylamide (191) is shown in Scheme Sixtytwo, in which ejection of a phenyl anion from the arsonium salt by a butyl anion is followed by ring opening. This is supported by the observation of Seyferth and co-workers[144] who found that treatment of methyltriphenylphosphonium bromide with methyllithium gave less than a full equivalent of methane but did produce 21-26% of benzene, apparently by phenyl anion ejection via a pentacovalent intermediate.

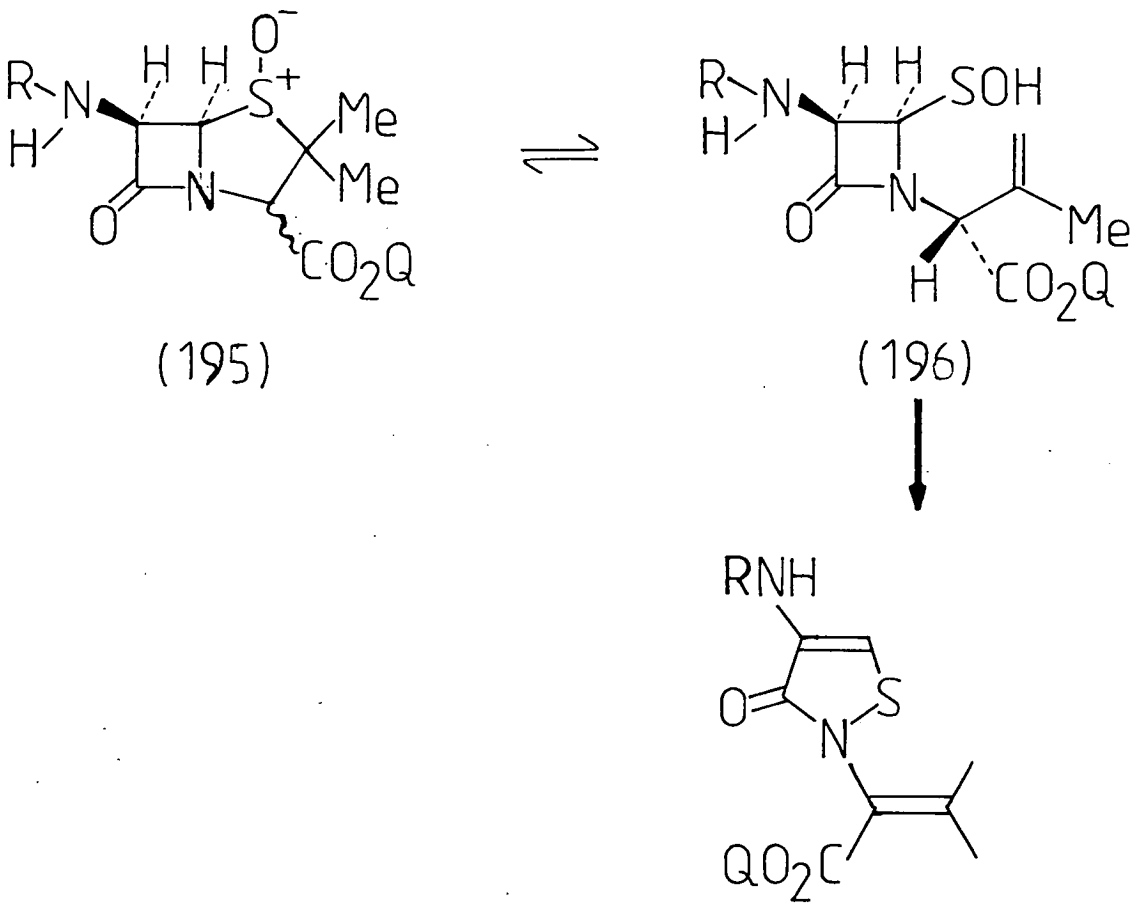
2.2 Formation of 1,3-thiazines from N-substituted-3-isothiazolones by internal ylide formation

2.2.1 Introduction

The ring expansion of 3-isothiazolones to 1,3-thiazines has not been exploited, although as mentioned earlier Gosney[130] observed the formation of (156) in the base-catalysed condensation of ethyl propiolate with N-ethyl-3-isothiazolone. By contrast, the reverse reaction of ring contraction has been widely reported by various authors. For example, Morin and Spry[145] obtained the isothiazolone (193) as the major product upon heating the benzothiazine sulphoxide (192; R=Me) in boiling acetic anhydride. In the case of the N-Me substituted benzothiazine (192; R=Me) the corresponding reaction gave the thiazepine (194) as the principle product instead of an isothiazolone.



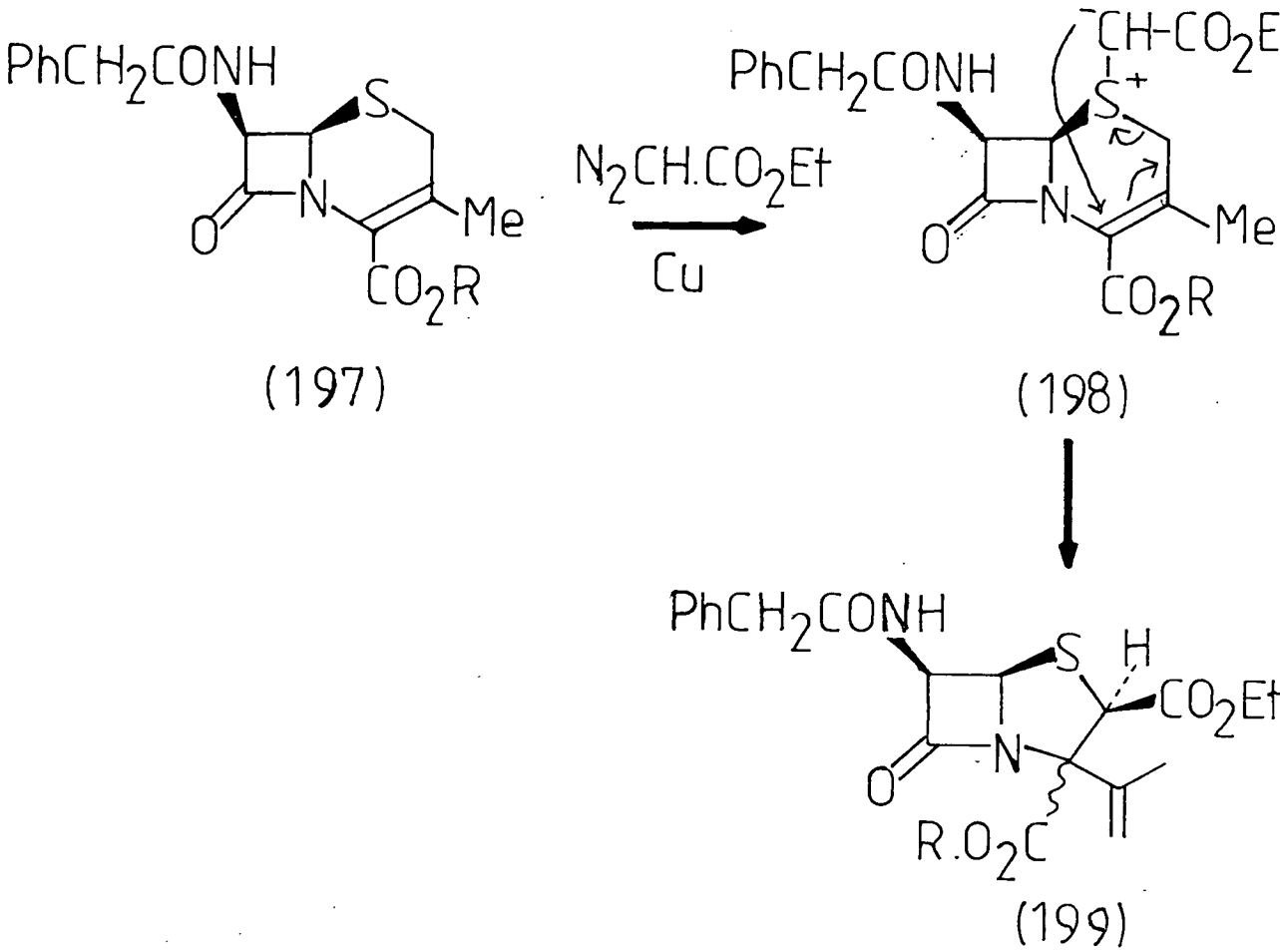
Several groups have also reported the base-catalysed conversion of penicillin sulphoxides (195) into isothiazolones. A typical rearrangement is shown in Scheme Sixtythree and is thought to involve the intermediacy of a sulphenic acid (196) followed by scission of the labile β-lactam ring[146-149].



Scheme Sixtythree

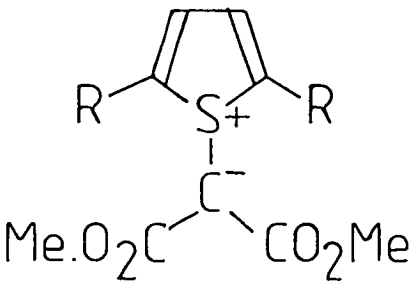
Amongst other skeletal rearrangements of particular interest is that reported by Yoshimoto and co-workers[150] involving conversion of a cephalosporin derivative (197) into the penicillin (199) by reaction with a carbene. The reaction is thought to involve a [2,3]-sigmatropic rearrangement of a sulphonium ylide intermediate (198) as depicted in Scheme Sixtyfour. The conversion of (198) into (199) utilises the well-known rearrangement of allylic

sulphonium ylides as the driving force for the reaction[8,150].



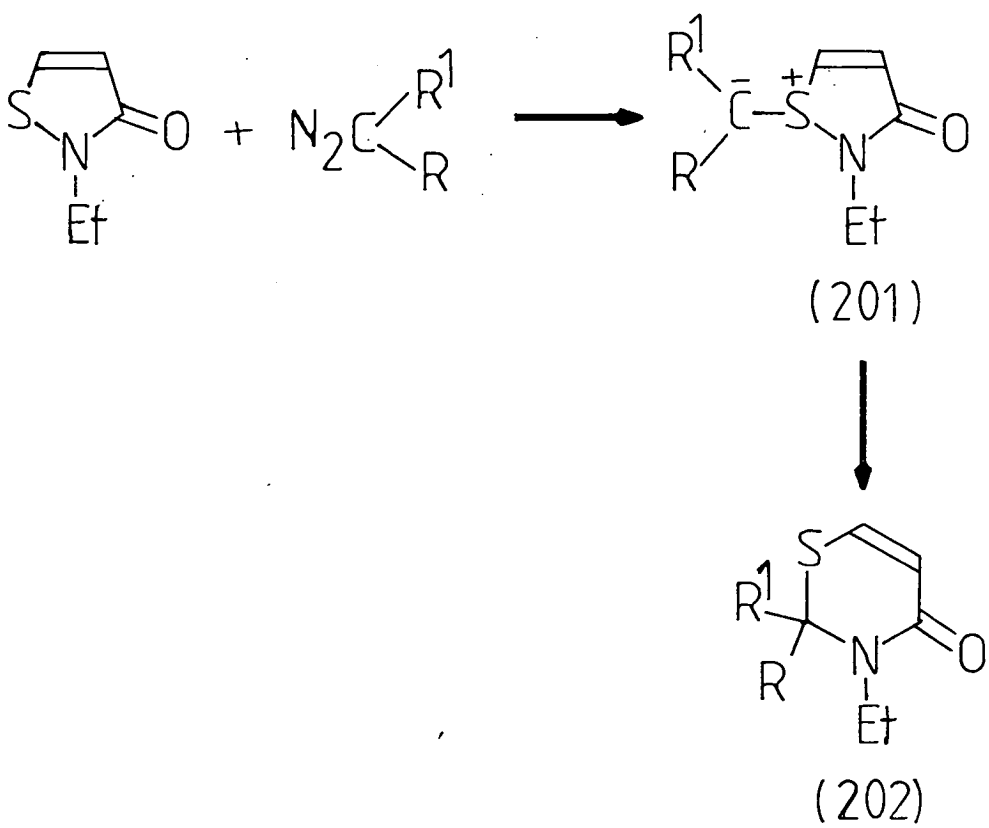
Scheme Sixtyfour

This reaction of sulphides with diazo compounds to generate sulphonium ylides is well known and has been reviewed by Ando[8]. In a recent typical example Porter and co-workers[151-154] have obtained the relatively rare class of sulphonium ylide[8], namely, thiophenium ylides (199), from the metal-catalysed decomposition of diazo malonate in the presence of the requisite thiophene. These workers found that the 2,5-dichloro derivative (200, R=Cl) served as a useful precursor for bis(carbomethoxy)carbene which could be trapped by suitable olefins[153].



(200)

The similar generation of a sulphonium ylide (200) from the reaction of an electrophilic carbene with N-ethyl-3-isothiazolone followed by ring-expansion (Scheme Sixtyfive) might be expected to give access to a 1,3-thiazine (202). Support for this approach is found in a report by Ando[155] of the reaction of 2,4-dihydrothiophene (203) with dimethyl diazomalonate leading to the ring expansion product (204)[155].



Scheme Sixtyfive

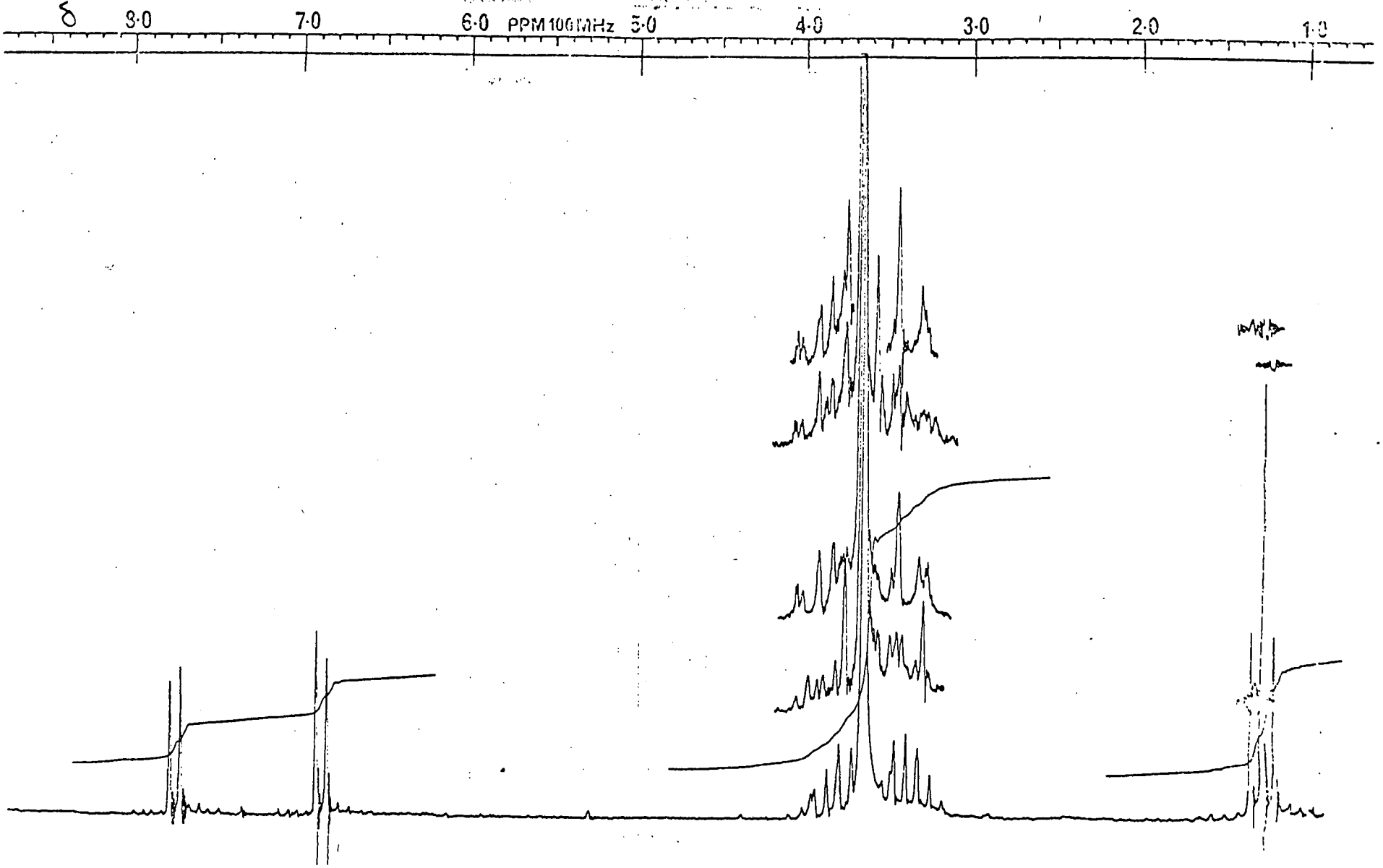
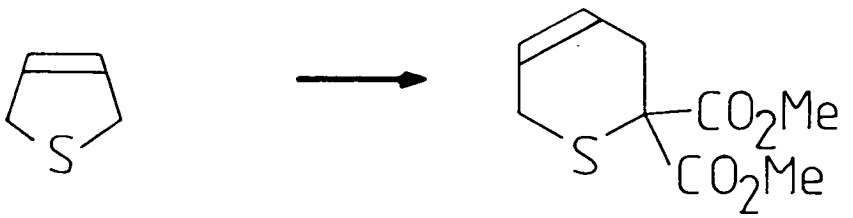


Figure 3. ^{1}H n.m.r. spectrum of (205).



(203) (204)

2.2.2 Reaction of N-ethyl-3-isothiazolone with electrophilic carbenes

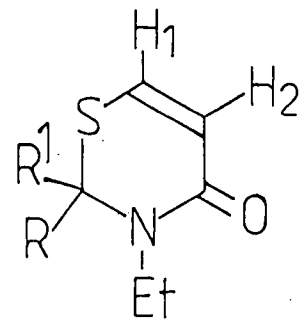
The rhodium (II) acetate catalysed decomposition* of dimethyl diazomalonate in the presence of an approximately equimolar amount of N-ethyl-3-isothiazolone in boiling benzene afforded a colourless compound which was identified as 2,2-bis(carbomethoxy)-3-ethyl-4-oxo-1,3-4H-thiazine (205). Elemental analysis gave percentage compositions for carbon, hydrogen and nitrogen consistent with an empirical formula $C_{10}H_{13}NO_5S$. This was verified by observation in the mass spectrum of a parent ion peak at m/e 259.

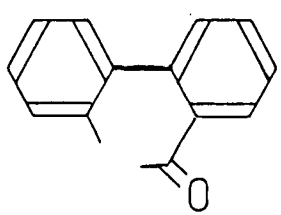
The ^1H n.m.r. spectrum of the product is shown in Figure 3. The structurally significant peaks are located at δ7.75 and 6.89, two one proton doublets (J = 6 Hz) and δ3.62, a six proton singlet. The cyclopropane structure

* The reaction mixture was initially blue-green in colour. A purple colour developed during the reaction, indicating that the efficiency of the catalyst was decreasing. T.l.c. was used to monitor all of the decomposition reactions.

Table 7. Olefinic ^1H n.m.r. assignments for 1,3-thiazines

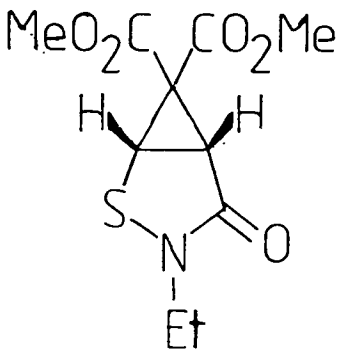
(All spectra recorded using $CDCl_3$ solutions).



	R	R^1	Yield	M.Pt./°C	δ(ppm from TMS) H_1	H_2	J/Hz
(205)	$-CO_2Me$	$-CO_2Me$	70	133.5-135.0	7.75	6.89	6
(206)	-COMe	-COMe	58	127.5-128	7.50	6.92	6
(207)	$-CO_2Et$	-COMe	74	120.5-121.5	7.45	6.87	6
(208)	$-CO.CH_2C(CH_3)_2CH_2CO-$		65	116-117	7.54	6.93	6.6
(209) *	$-CO.O-C(CH_3)_2O.CO-$		74	162.5-163	7.62	7.05	6
(210)			91	148-149.5	6.28	6.07	5.8

*see Figure 4 for ^1H n.m.r.

(211) was ruled out because of the absence of cyclopropane protons and the retention of olefinic doublets in the ^1H n.m.r. spectrum.



(211)

Table 7 lists the yields, melting points and ^1H n.m.r. data for other 1,3-thiazines obtained from the catalysed decomposition of: 2-diazo-5,5-dimethylcyclohexan-1,3-dione, Meldrum's diazo, diazoacetylacetone, diazo ethylacetoacetate and 9-diazo-10-phenanthrenone, in the presence of N-ethyl-3-isothiazolone. The olefinic proton chemical shifts for the 1,3-thiazines compare favourably with those reported in the literature (see Table 8).

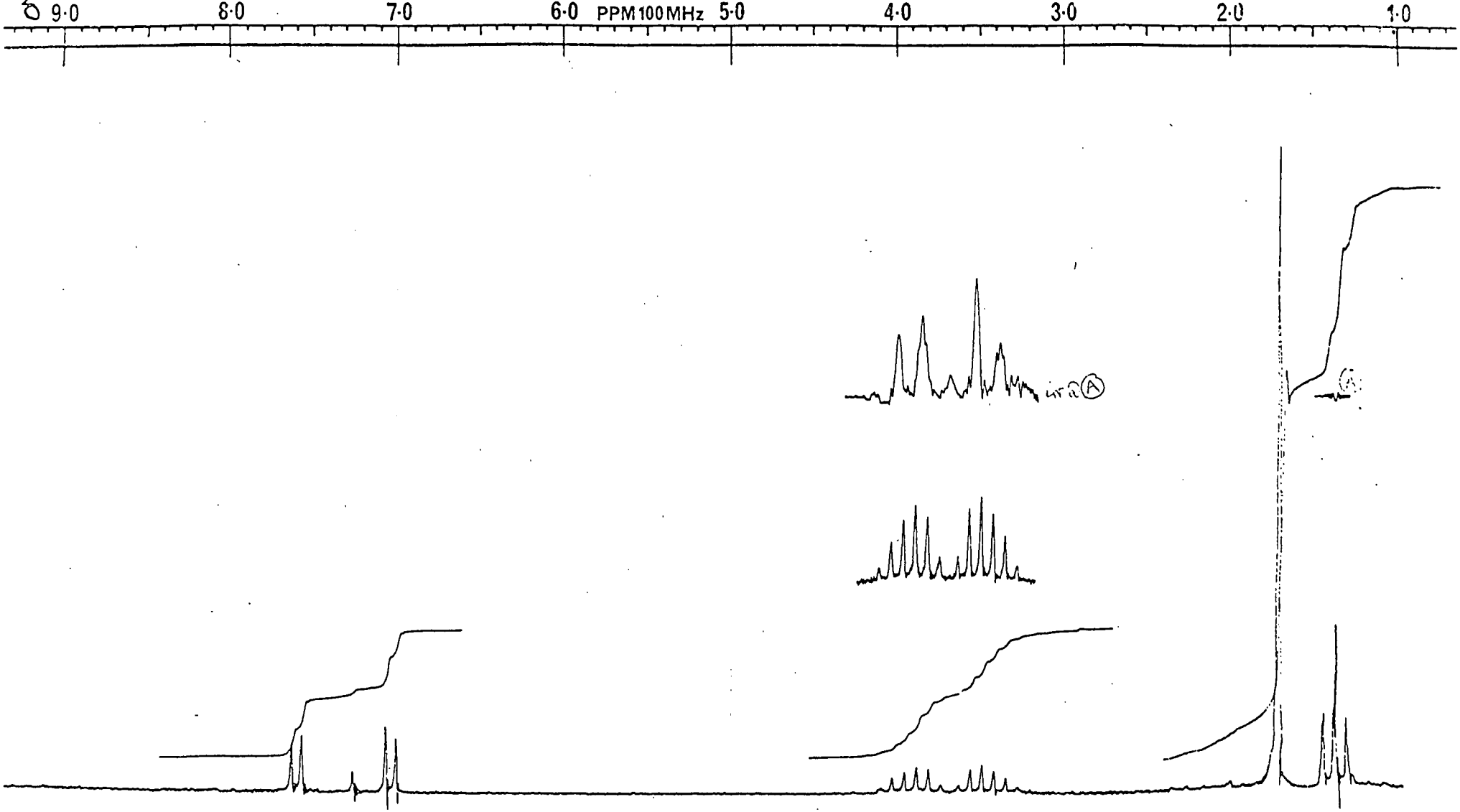
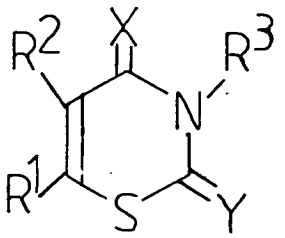
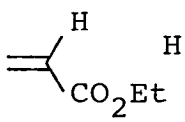


Figure 4. 100 MHz ^{1}H n.m.r. spectrum of (209).

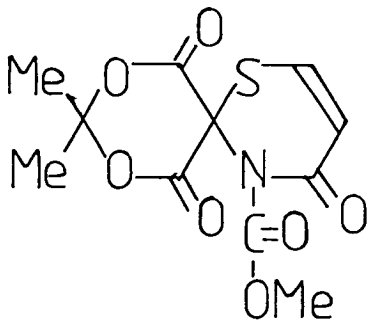
Table 8. ^1H n.m.r. data for 1,3-thiazines



X	Y	R^1	R^2	R^3	H_6	H_5	$J_{6,5}$
O[156]	S	H	H	H	7.86	6.68	10.4
S[156]	S	H	H	H	7.64	7.26	10.2
O[157]	O	H	H	CH_3	7.37	6.5	10.2
O[157]	O	CH_3	H	H	-	6.32	-
O[130]		H	H	Et	7.21	6.26	10.5

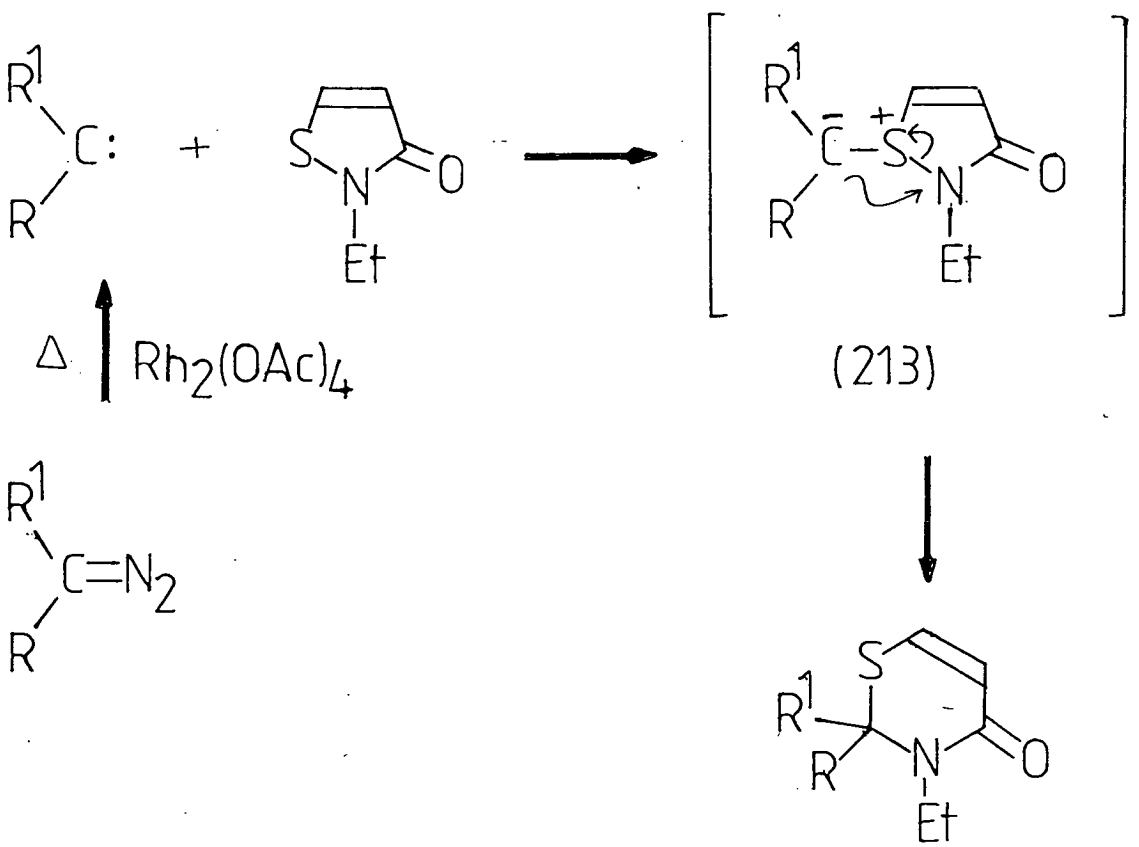
The amino methylene protons of the 1,3-thiazines (205), (206), (207), (208) and (209) exhibited a complex multiplet in their ^1H n.m.r. spectra. Irradiation of the methyl protons led to the collapse of this multiplet to an AB-quartet. The presence of this AB-quartet is presumably due to steric interactions with the 2-carbonyl groups or slow inversion at the amide nitrogen atom[158].

The more reactive substrate, N-carbomethoxy-3-isothiazolone (152, R = CO_2Me) reacted with the carbene from Meldrum's diazo in the normal manner to give (212) in 95% yield.



(212)

From a mechanistic viewpoint thiazine formation can be ascribed to the trapping of a carbene or carbenoid species to yield an intermediate sulphonium ylide (213) which undergoes a 1,2-shift as shown in Scheme Sixtysix.

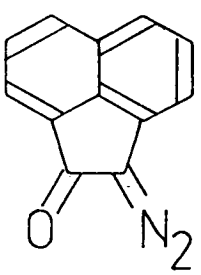


Scheme Sixtysix

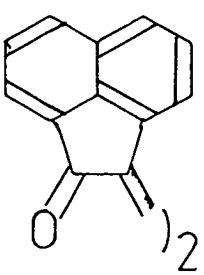
Several diazo compounds namely, ethyl diazoacetate, 4,4^1-di-tert-butylbenzoylphenyldiazomethane and 1-diazo-2,3,4-triphenylcyclopentadiene, failed to decompose in the presence of rhodium (II) acetate. It appears that in these

cases the initial diazo-metal complex (carbenoid species) was insufficiently reactive towards N-ethyl-3-isothiazolone due to steric hindrance or perhaps poor carbene electrophilicity.

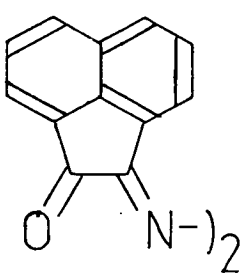
Catalytic decomposition of 2-diazoacenaphthen-1-one (214) in the presence of N-ethyl-3-isothiazolone gave the carbene dimer (215), rather than the thiazine, in almost quantitative yield with 82% recovery of the isothiazolone. Ried[159] has reported that thermolysis of (214) in boiling absolute xylene gives chiefly (215), and a slight amount of the ketazine (216), whereas thermolysis of molten (215) affords chiefly (216). De Jongh and van Fossen[160]



(214)

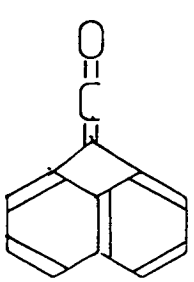


(215)



(216)

obtained (215) on pyrolysis of (214) at 160°C. In passing it might be noted that the reluctance of (214) to undergo a Wolff rearrangement is presumably due to the great increase in strain which would occur on forming the ketene (217).



(217)

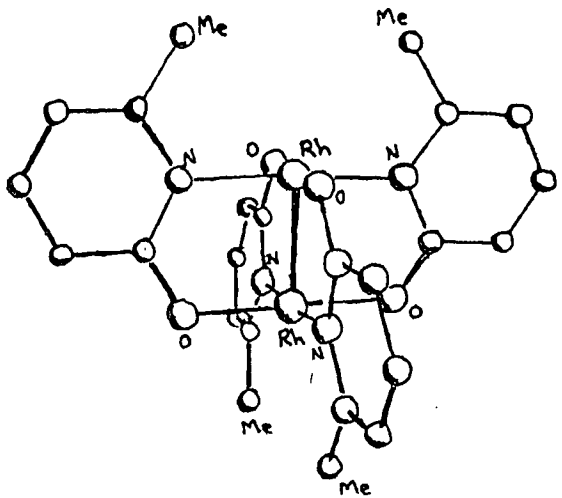


Fig. 6 Molecular structure of $Rh_2(mhp)_4$

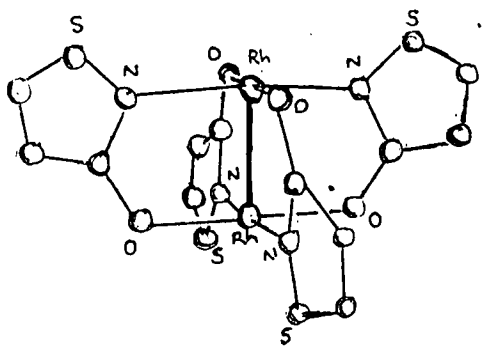
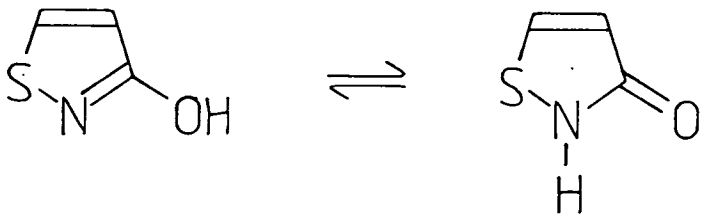


Fig. 5 Molecular structure of (219)

2.2.3 Reaction of 3-isothiazolone with electrophilic carbenes

The corresponding decomposition of diazo compounds in the presence of 3-isothiazolone (152, R=H) failed to yield a 1,3-thiazine. For example, when Meldrum's diazo and 3-isothiazolone were treated with a catalytic amount of rhodium (II) acetate in boiling benzene, the initial green colour of the solution turned red, but t.l.c. indicated that no reaction had taken place. Following the addition of more catalyst, the reaction mixture was cooled whereupon a red precipitate deposited out of solution. The characteristic smell of acetic acid in the solution indicated that the catalyst had decomposed. Elemental analysis and mass spectral data showed that the red crystals contained carbon, hydrogen and nitrogen, apparently as the 3-isothiazolone anion. The infrared spectrum of the solid exhibited only one carbonyl stretching frequency (1630 cm^{-1}) and no NH or OH absorption. On the basis of this data, the red complex was assigned the structure (219) (Figure 5) with D_{2d} symmetry similar to that found by Garnerand co-workers[161] for tetrakis-(6-methyl-2-oxopyrimidinato)dirhodium (218) (Figure 6). The ability of 3-isothiazolone to act as an ambidentate ligand is presumably a consequence of the lactim-lactam tautomerism previously demonstrated by Crow and his co-workers[133] (see Scheme Sixtyseven).

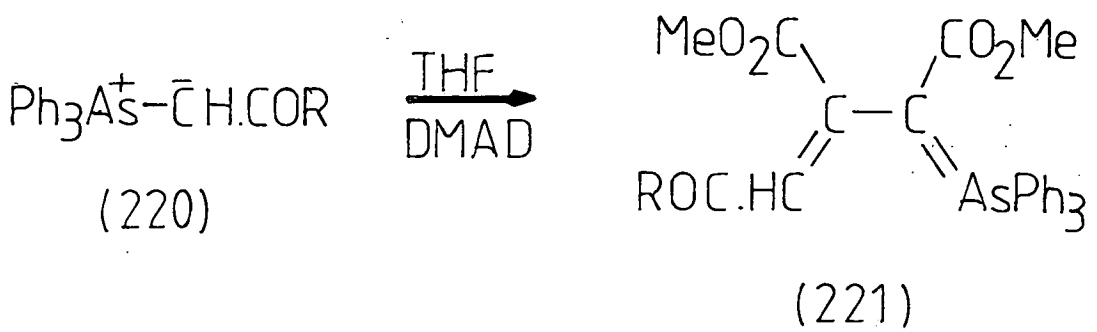


Scheme Sixtyseven

2.3 Reaction of arsonium ylides with acetylenes

2.3.1 Introduction

In the only report to date concerning the reaction of arsonium ylides (220) with dimethyl acetylenedicarboxylate, Trippett and Walker[30] obtained the rearrangement products (221) in tetrahydrofuran.

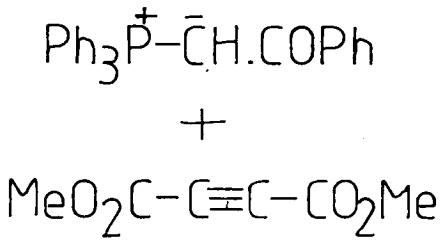


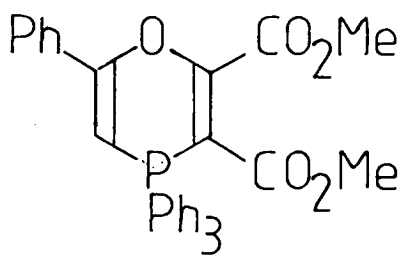
(220) (221)

R = OEt, C_6H_4-Br-p

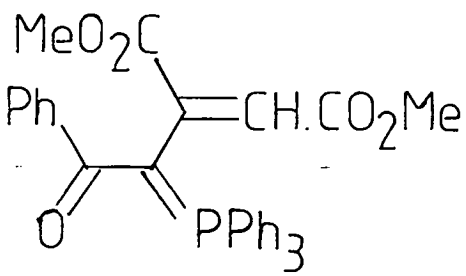
By comparison, the reaction of phosphonium ylides with acetylenic esters has been studied by several groups. In 1961, Hendrickson reacted triphenylphosphonium phenacylide with dimethyl acetylenedicarboxylate in methanol and obtained a 1:1 adduct for which he proposed the cyclic phosphoranyl structure (222)[162]. However, in connection with their ylide pyrolysis experiments, Gough and Trippett[163] proposed that the ylide (222) would be a

more likely structure, especially as they found that the adduct lost triphenylphosphine oxide on pyrolysis to give the acetylene (224).

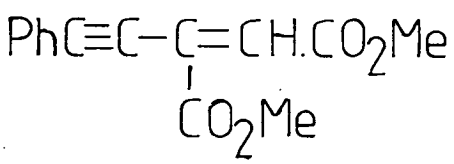




(222)

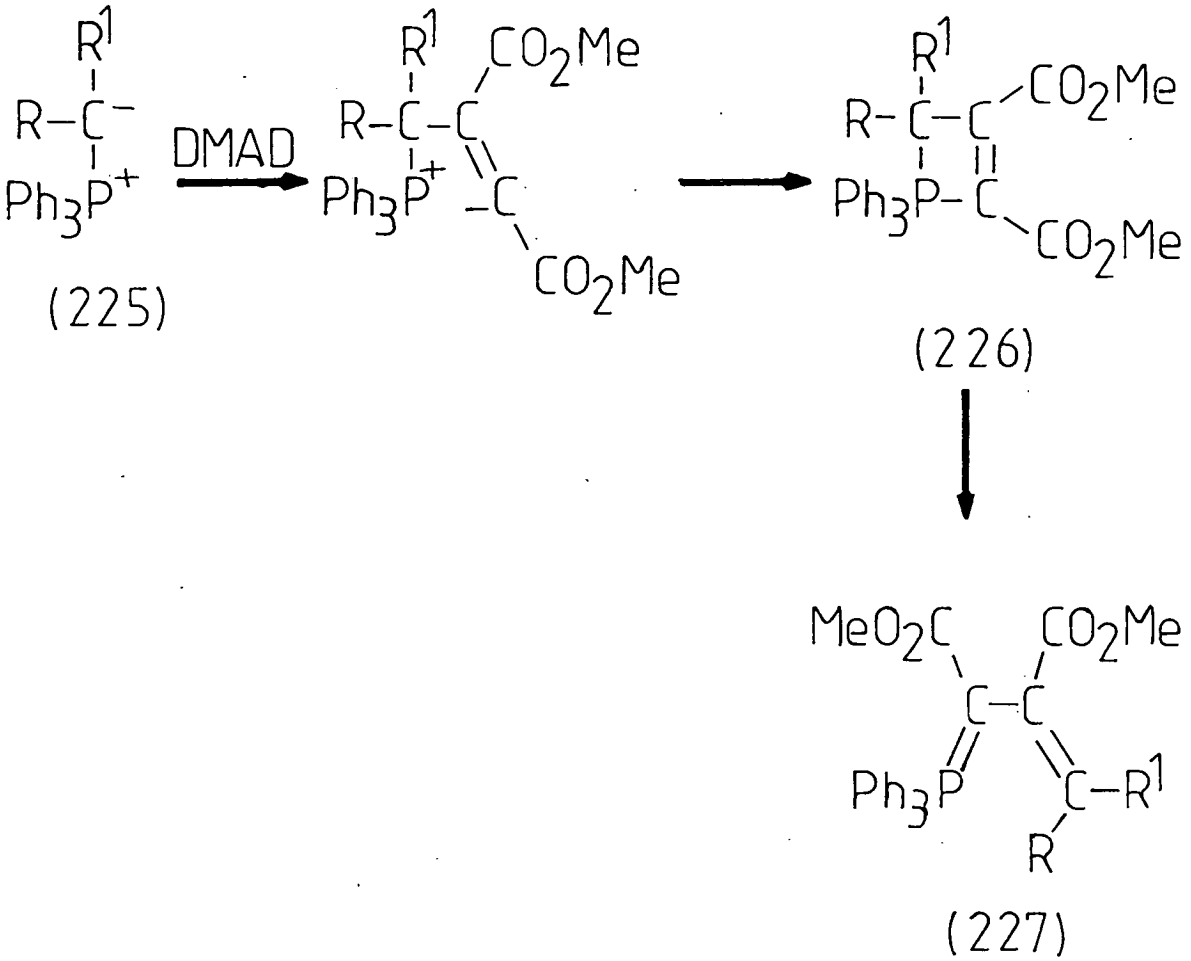


(223)



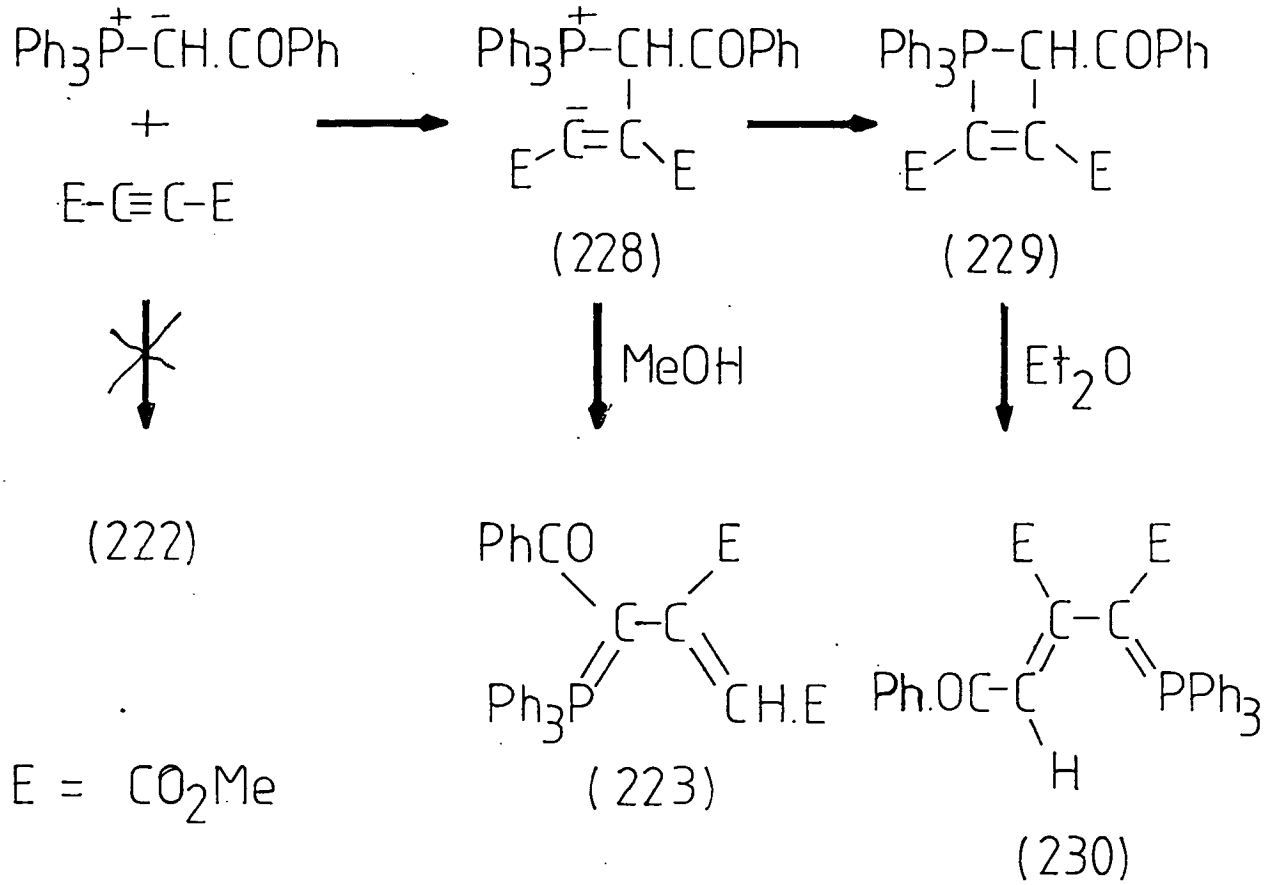
(224)

Bestmann and Rothe[89] further investigated this reaction and reported that triphenylphosphonium alkylides (225) condensed with dimethyl acetylenedicarboxylate to yield the rearrangement products (227) by way of a four-membered cyclic intermediate (226) (Scheme Sixtyeight). The authors failed to mention the solvent (if any) used.



Scheme Sixtyeight

In 1965, Hendrickson and co-workers[88] retracted the structure (222), and reported that the reaction of triphenylphosphonium phenacylide with dimethyl acetylene-dicarboxylate was solvent dependent. In ether, an aprotic solvent, the reaction afforded the product (230), while in methanol, a protic solvent, (229) was obtained. They proposed that the first step in both solvents involved a Michael addition to give the intermediate (228), thereafter in methanol a proton shift occurred to give (223), while in ether ring closure followed by ring opening gave the product (230) (Scheme Sixtynine). No previously reported cyclic phosphoranyl product (222) was obtained.



Scheme Sixtynine

2.3.2 Reaction with methyl propiolate

In view of the paucity of data available, it seemed worthwhile to investigate the reaction of stabilised arsonium ylides with unsymmetrical acetylenes in more detail, and to compare their behaviour with that of phosphorus analogues. Thus, when triphenylarsonium phenacylide (22) was boiled in methanol with an equimolar amount of methyl propiolate, a pale yellow crystalline product (m.p. 181-182°C dec) was formed in 53% yield. However, when the corresponding reaction in benzene was carried out, a different pale yellow crystalline product (m.p. 184-185°C) was obtained in 45% yield. Both compounds were isolated by column chromatography from alumina.

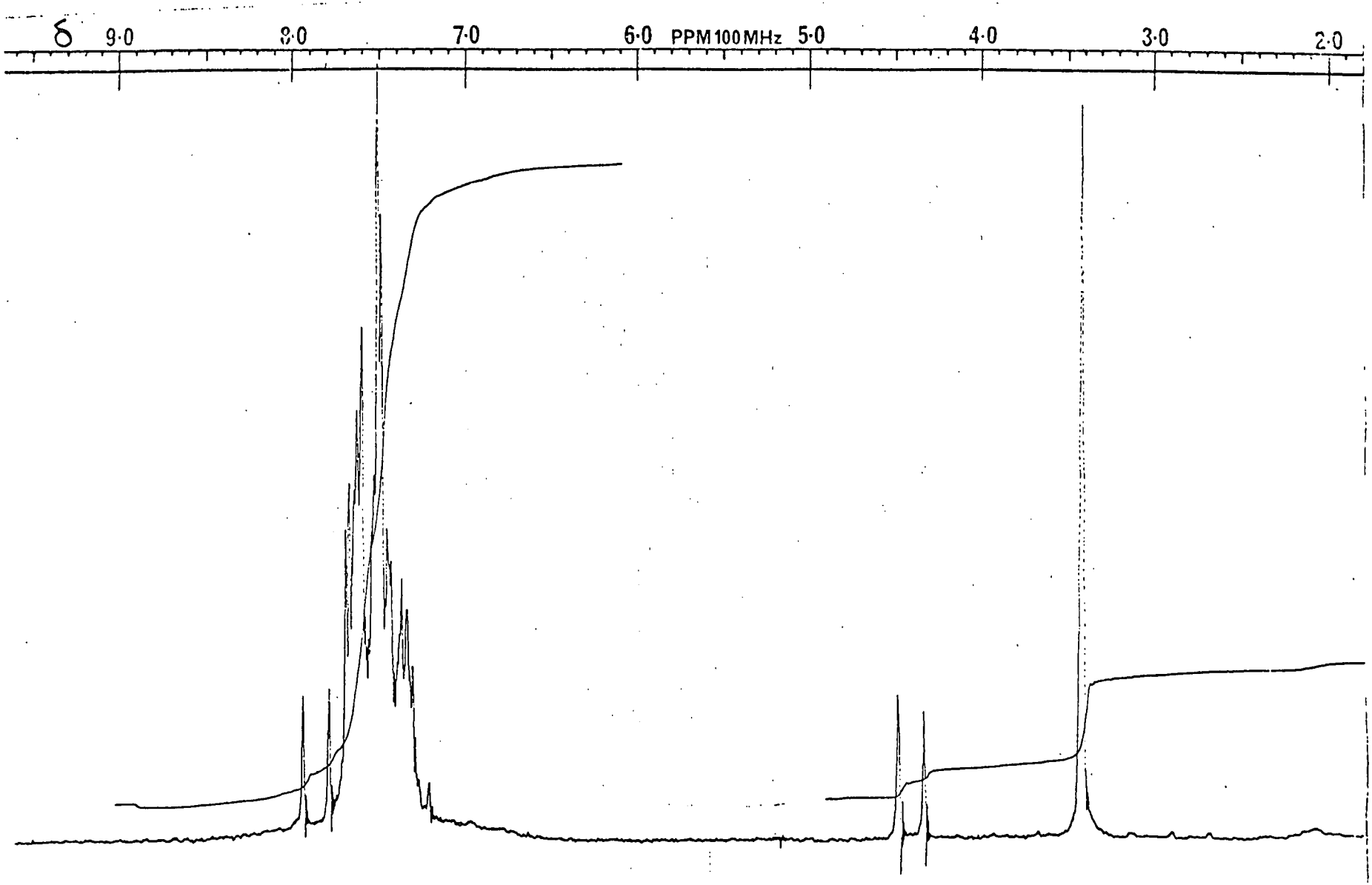
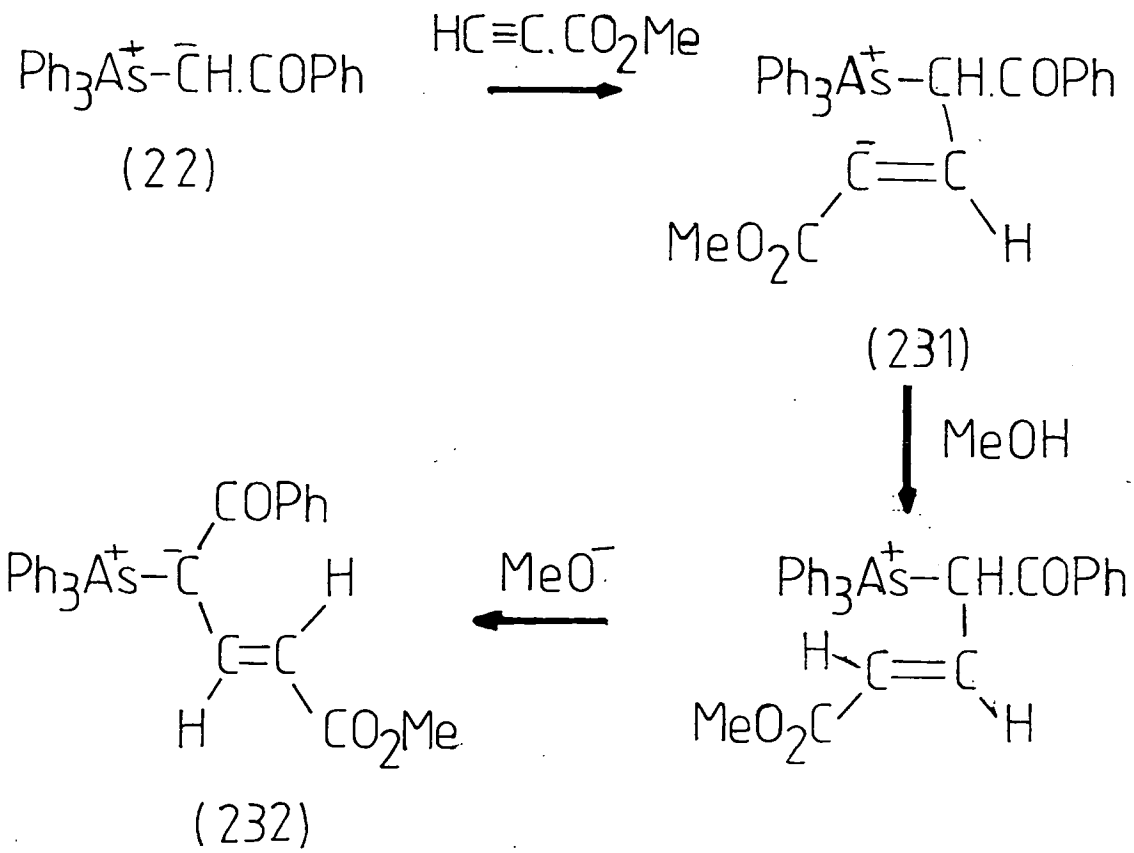


Figure 7. 100 MHz ^{1}H n.m.r. spectrum of (232).

Microanalyses and mass spectral data confirmed that the two products were isomeric 1:1 adducts with the empirical formula $C_{30}H_{25}AsO_3$.

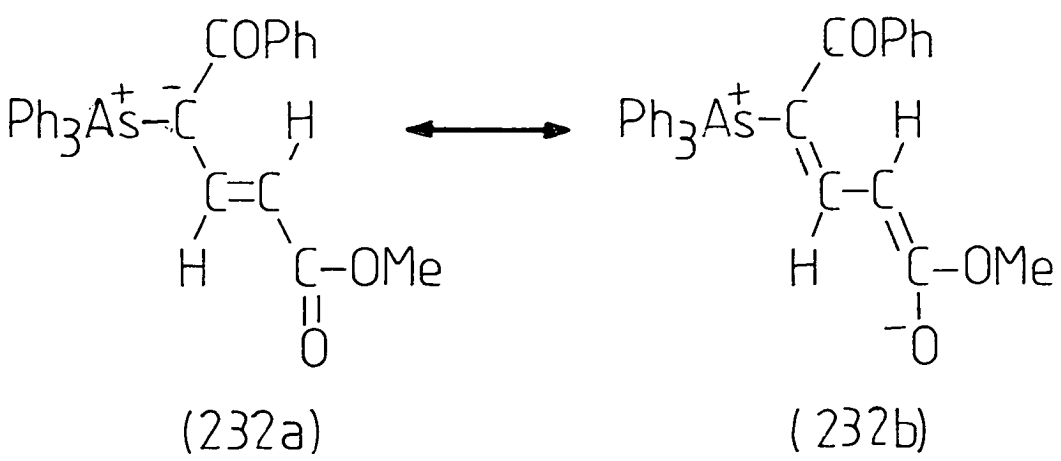
Examination of the adduct obtained in methanol by ^1H n.m.r. spectroscopy (Figure 7) showed the presence of an ester methoxyl singlet of three protons at δ3.42, a complex multiplet of twenty protons at δ7.7-7.3, and two single protons as doublets (J = 14 Hz) at δ7.89 and 4.42. These data are consistent with the structure (232), which can be envisaged as being formed by protonation then deprotonation of the Michael adduct (231) (Scheme Seventy). Corroboration of structure (231) was obtained from its i.r. spectrum which showed the presence of two carbonyl groups (ν_{max} 1686 and 1586 cm^{-1}).



Scheme Seventy

It is assumed that (232) is a trans adduct since it has been shown that, where mobile protons are available, the product of addition of triphenylphosphonium phenacylide to acetylenedicarboxylic esters is the simple trans adduct[88,164,165]. There seems to be no a priori reason for expecting different behaviour in the case of arsonium ylide attack on methyl propiolate.

The trans geometry about the olefinic double bond of ylide (232) was confirmed by the large coupling constant of 14 Hz between the two olefinic protons, c.f. cis-coupling 6-12 Hz[166]. The carbonyl stretching frequencies for triphenylarsonium phenacylide and triphenylarsonium carbomethoxymethylide are 1514 and 1608 cm^{-1},[53] respectively, while the carbonyl stretching frequencies for (232) are 1686 and 1586 cm^{-1}. Comparison suggests that the latter frequency is due to the phenacylide carbonyl. The former frequency is higher than that of the carbomethoxymethylide, but lower than that expected for an α,β-unsaturated ester (1750-1735 cm^{-1})[166]. This can be explained if the canonical form (232b) makes a significant contribution to the structure of the ylide.



(232a) (232b)

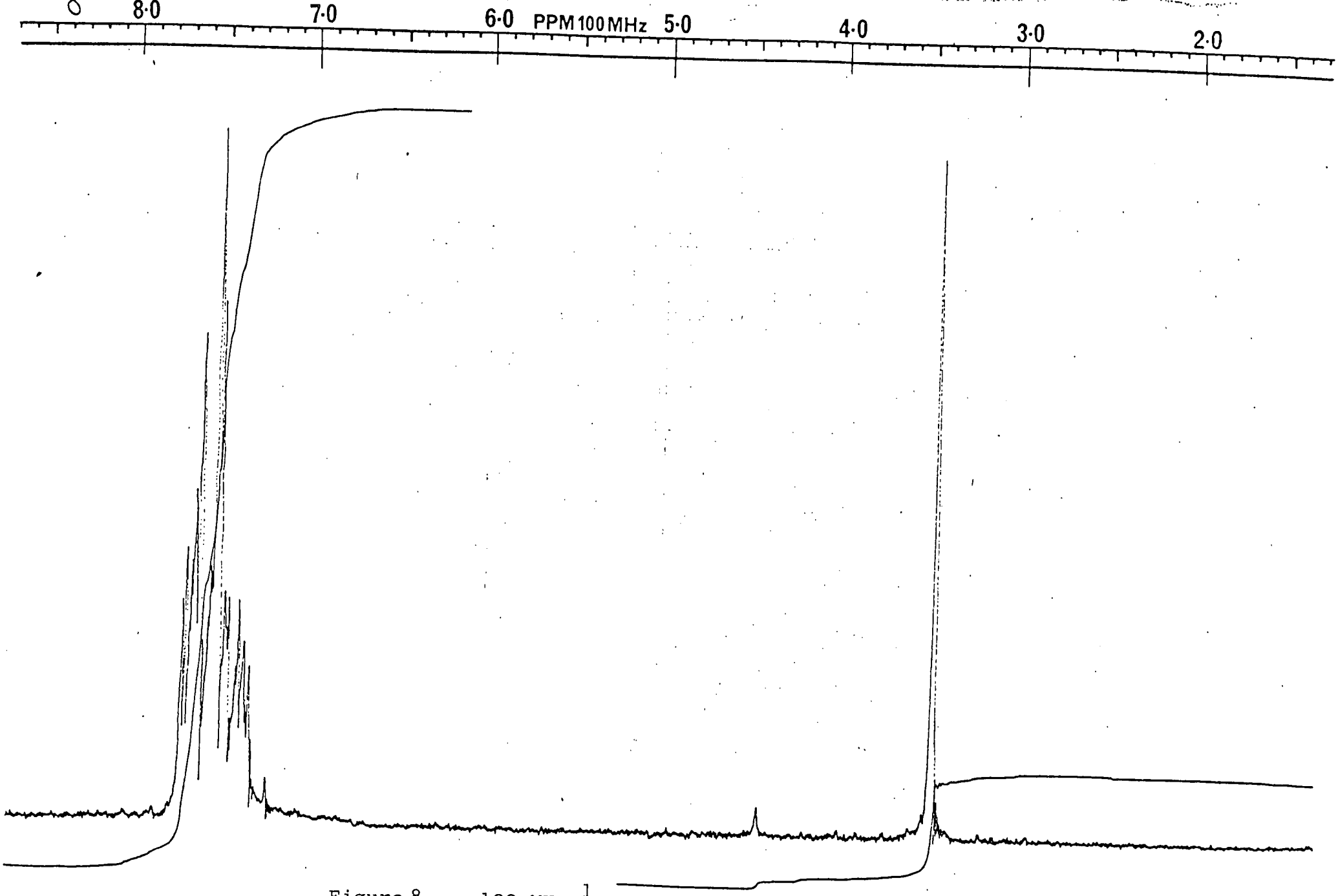
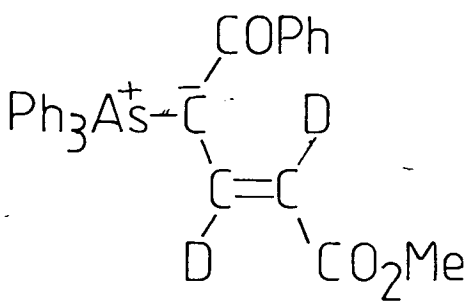


Figure 8 . 100 MHz ^{1}H n.m.r. spectrum of (233).

In an attempt to assign chemical shifts to the methine protons of ylide (232), labelling experiments were conducted using d'-methyl propiolate. However, the experiments failed to resolve the problem as no mono-deuterated product could be obtained. Thus, d^1-methyl propiolate was prepared by treatment of methyl propiolate with deuterium oxide to which was added a catalytic amount of sodium. Stirring of the heterogeneous system overnight achieved approximately 75% deuteration as evidenced by ^1H n.m.r. spectroscopy.

Reaction of triphenylarsonium phenacylide with d^1-methyl propiolate in methanol afforded only the non-deuterated adduct (232), whereas the corresponding reaction in d^4-methanol afforded the bis-deuterated ylide (233) exclusively. The ^1H n.m.r. spectrum of (233) is recorded in Figure 8 and shows one ester methoxyl singlet of three protons at δ3.42, and a complex multiplet of twenty protons at δ7.8-7.3



(233)

The spectra of the isomeric adduct formed in benzene differed markedly from those of the adduct (232). ^1H N.m.r. spectroscopy (Figure 9) showed the presence of

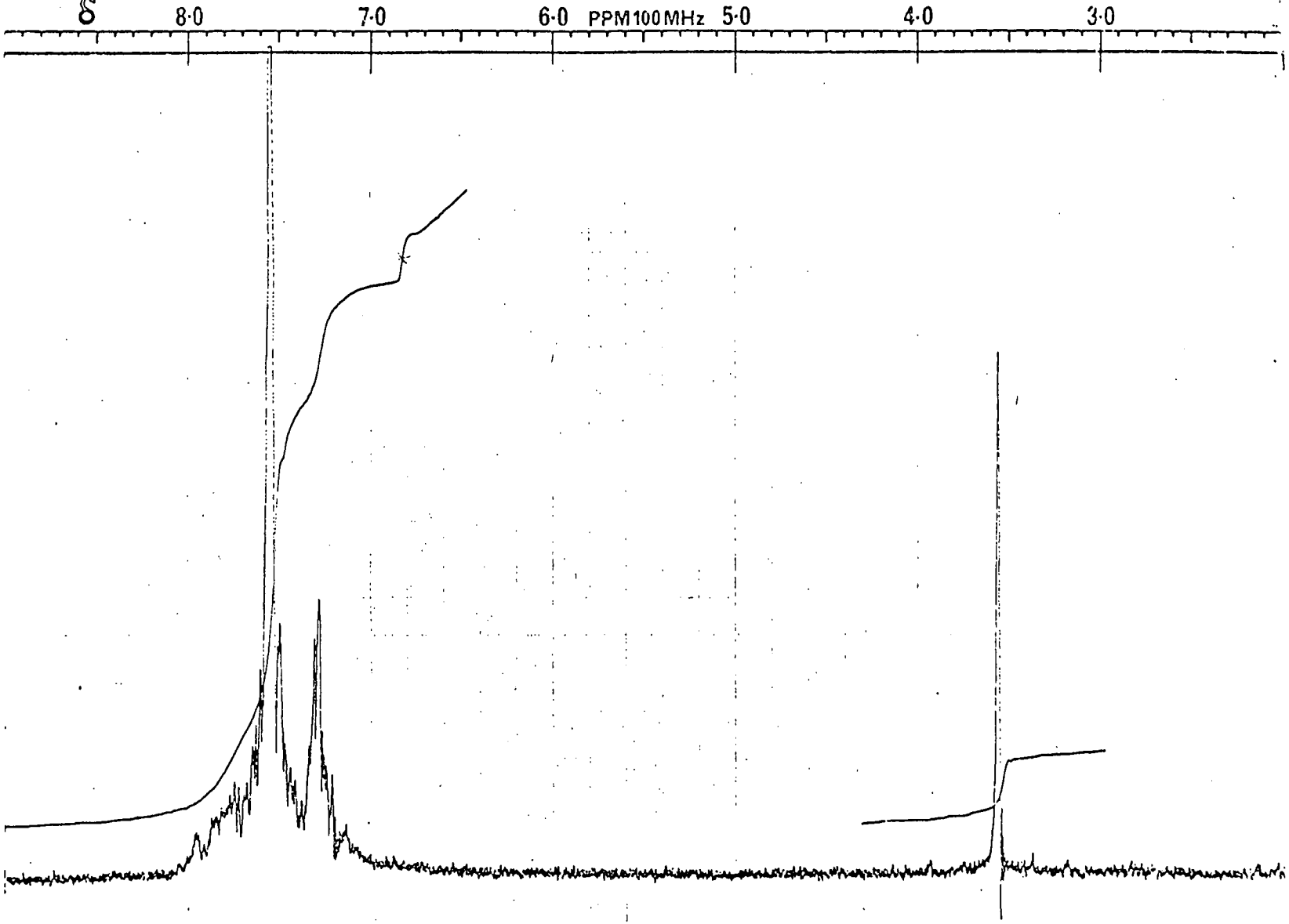


Figure 9. 100 MHz ^{1}H n.m.r. spectrum of (236).

a methoxy singlet of three protons at δ3.57, while the remaining twenty two protons were contained under a complex multiplet at δ8.1-7.1. Significantly, the i.r. spectrum showed only one carbonyl stretching frequency at 1670 cm^{-1}, indicating the loss of a carbonyl group, presumably that of the phenacyl group since the mass spectrum of the adduct showed the following peaks: m/e 508 (p^+), 477 (p^+-OMe) and 449 (p^+-CO_2Me).

The adduct reacted with an equimolar amount of dimethyl acetylenedicarboxylate in boiling benzene to afford the ylide (56c) together with a compound of the empirical formula $C_{18}H_{16}O_6$, in poor yields. The ylide (56c) was identified by comparison of its spectral data with those reported by Ciganek[50] for the product from the reaction of triphenylarsine oxide with dimethyl acetylenedicarboxylate (see Introduction, Scheme Thirteen). Reaction of the original adduct with two molar equivalents of dimethyl acetylenedicarboxylate afforded both products in much improved yield (>80%).

On the basis of its ^1H n.m.r. spectrum, the compound of formula $C_{18}H_{16}O_6$ was identified as trimethyl 1,1^1-biphenyl-2,4,5-triscarboxylate (234). The ^1H n.m.r. spectrum (Figure 10b) showed the <u>para</u> aromatic protons of the tetrasubstituted ring as one proton singlets at δ8.21 and 7.67, and three methoxyl groups as three proton singlets at δ3.91, 3.93 and 3.67. The i.r. spectrum showed the required ester absorptions at 1748, 1735 and 1722 cm^{-1}. The presence of three carbomethoxyl groups in (234) was further evidence that the arsenic-containing adduct contained an ester grouping, and that

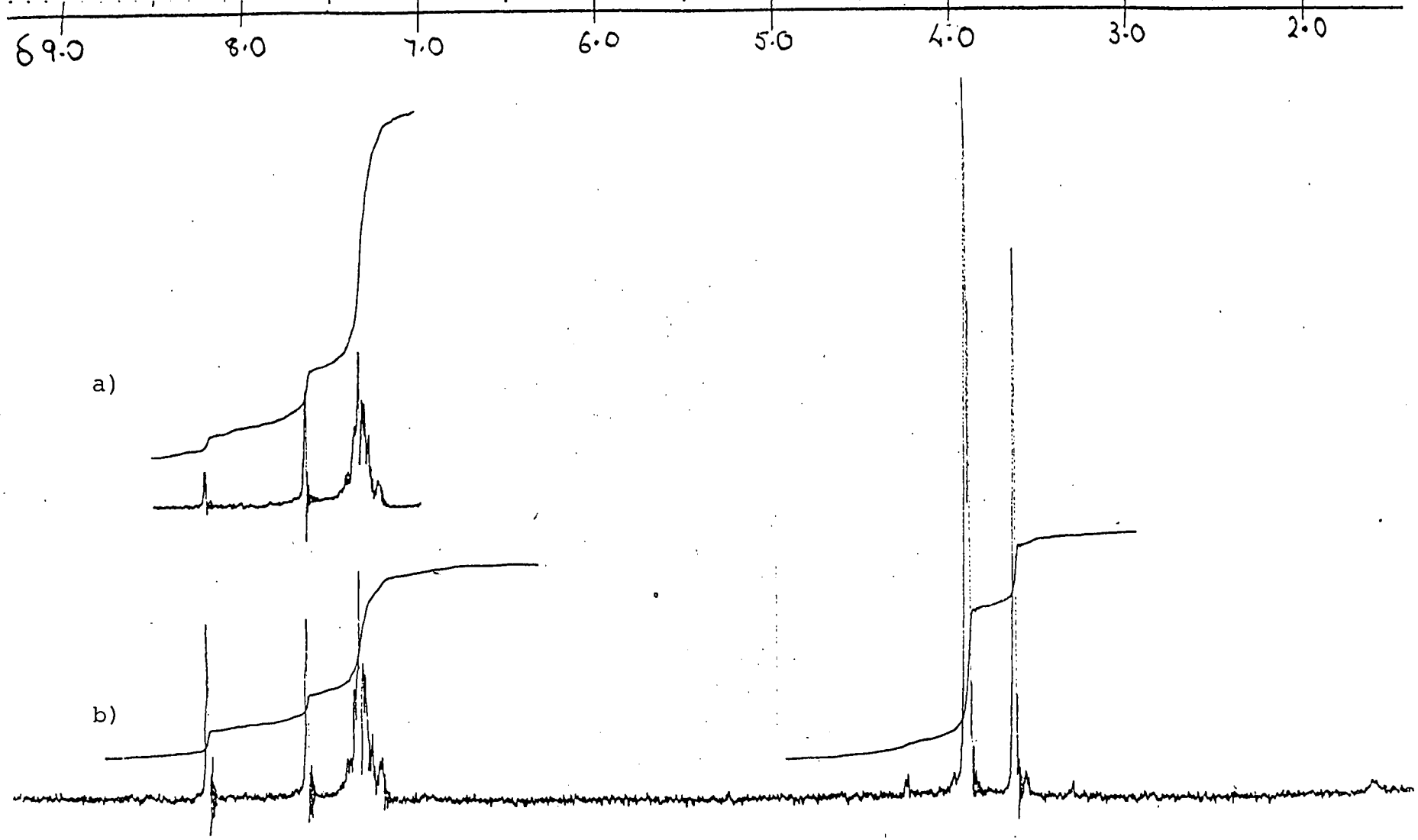
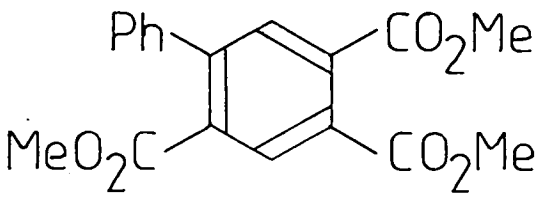


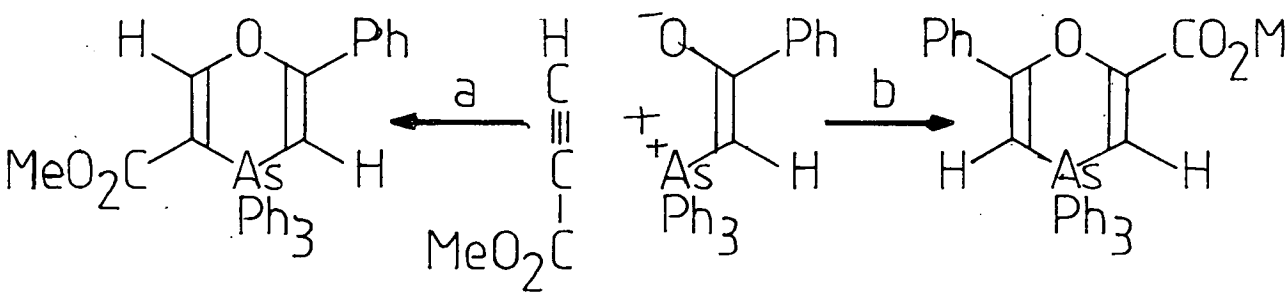
Figure 10 100 MHz ^{1}H n.m.r. spectrum of (234).

the phenacyl group was lost during its formation.



(234)

From this evidence it seems reasonable to assume that the initial adduct could have been formed by a [4+2] cycloaddition reaction of the ylide with methyl propiolate as outlined in Scheme Seventyone. However, two structures are possible, both of which conform to the spectral data available.

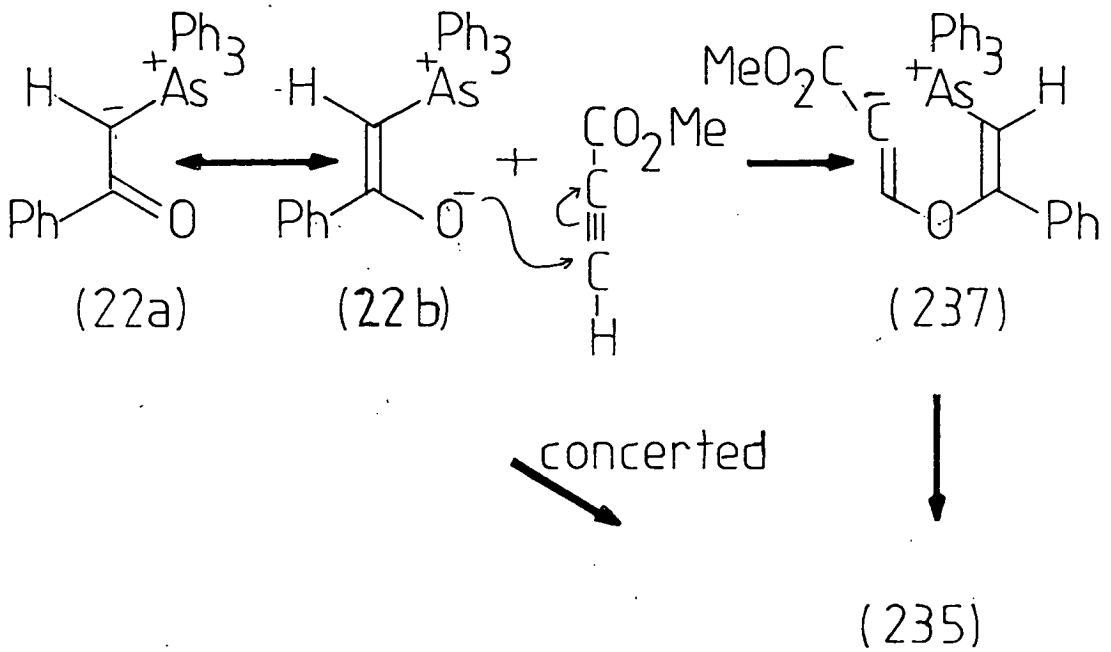


(235) (236)

Scheme Seventyone

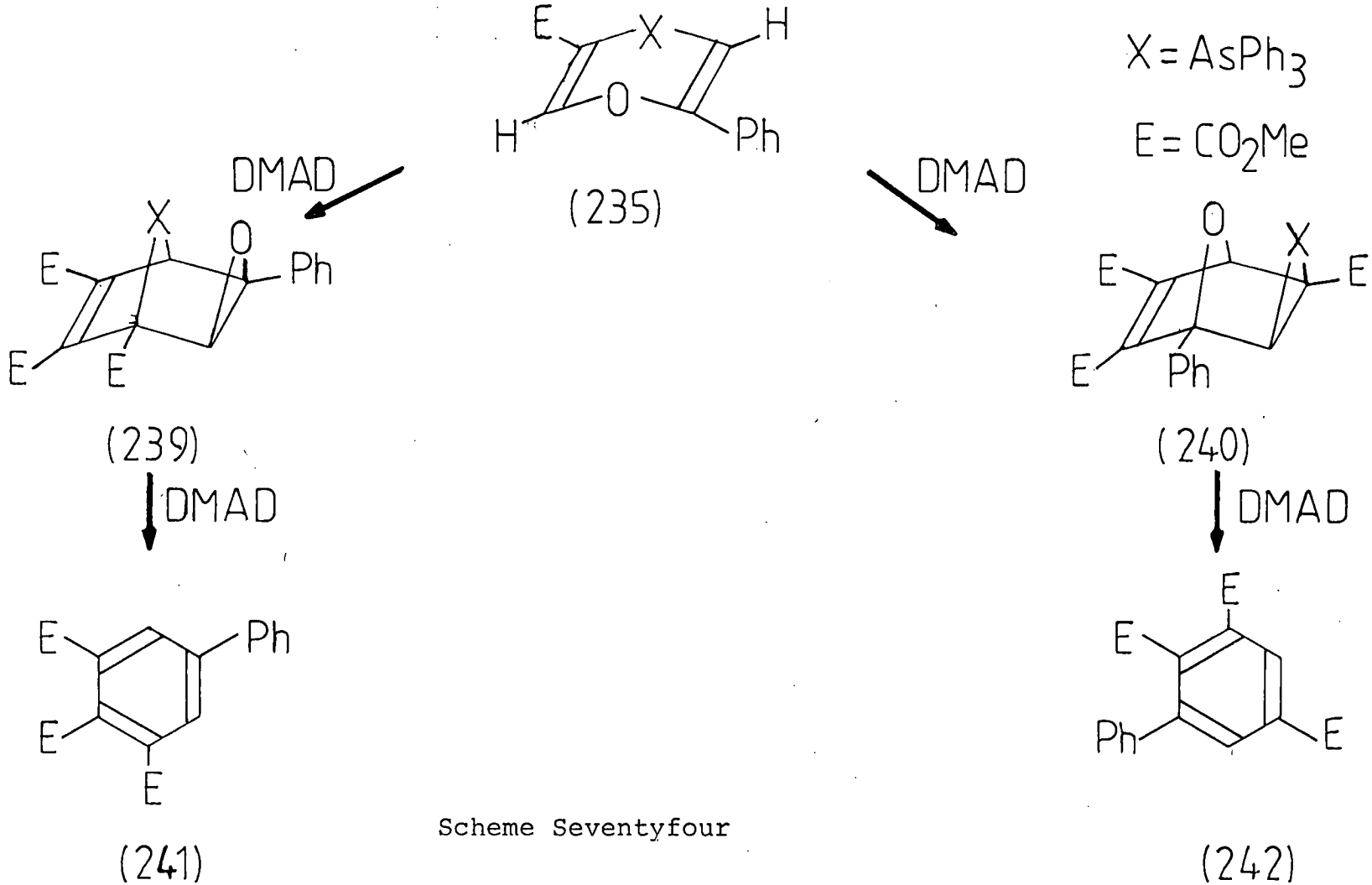
Several mechanisms can be envisaged for the formation of the adducts (235) and (236) other than a Diels Alder reaction. For example, the triphenylarsonium phenacylide can be considered as a 1,4-dipole (22b), which

in a Michael attack on the methyl propiolate affords the intermediate (237) and subsequently (235) by ring closure (Scheme Seventytwo). This pathway is

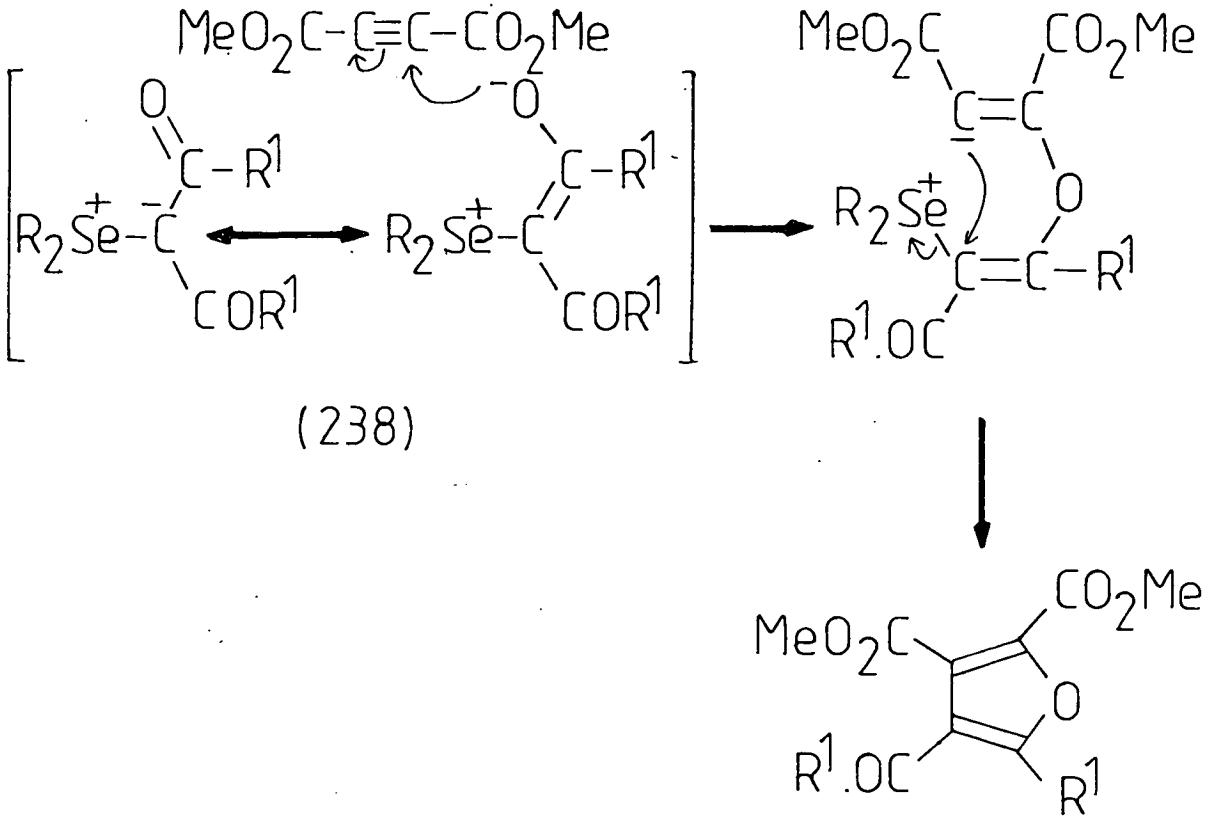


Scheme Seventytwo

analogous to that proposed for the formation of furans from the reaction of selenonium ylides (238) with dimethyl acetylenedicarboxylate[167,168]. Presumably the first step of the reaction is attack on the acetylene moiety by the acyl oxygen, rather than by a carbon atom, as shown in Scheme Seventythree.



Scheme Seventyfour

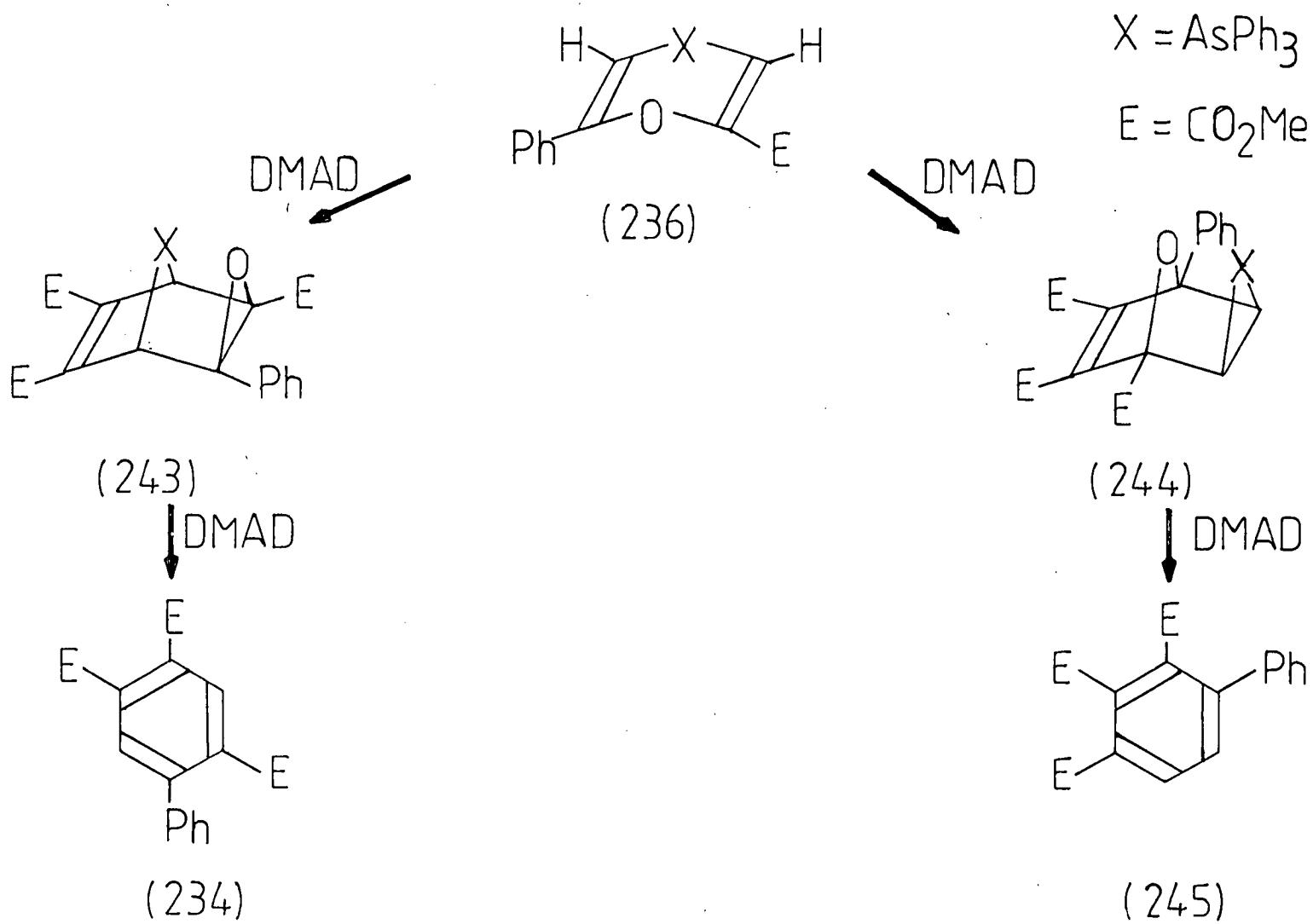


(238)

Scheme Seventythree

Similarly, Gosney and Lloyd[40] have shown that triphenylarsonium phenacylide reacts with diphenylcyclopropenone to afford 3,4,6-triphenyl-2-pyrone (see Section 1.4.1). Again, attack by the acyl oxyanion was assumed to be the initial step in the reaction pathway.

Reaction of the arsoranes (235) and (236) with dimethyl acetylenedicarboxylate, with subsequent loss of triphenylarsine oxide, can be expected to proceed in one of two ways (see Schemes Seventyfour and Seventyfive). For either arsorane, the acetylene can add across the C-As-C unit or the C-O-C unit. To accommodate a pentacovalent arsenic atom, an oxygen atom, and two olefinic double bonds in a six-membered ring, as in (235)



Scheme Seventyfive

and (236), a boat-like conformation must be adopted (Figure 11), as shown by molecular models. Hence, the dimethyl acetylenedicarboxylate adducts, (239), (240), (243) and (244), will each have the triphenylarsine moiety and the epoxide oxygen on the same side of the molecule (Figure 12).

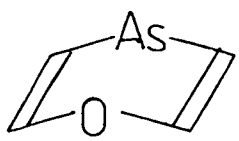
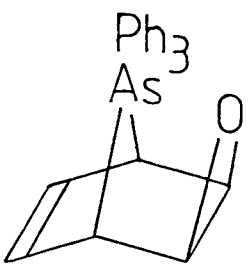
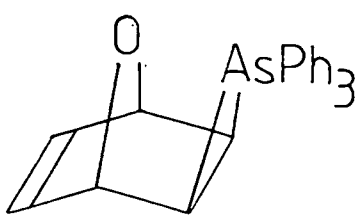


Figure 11



(a)

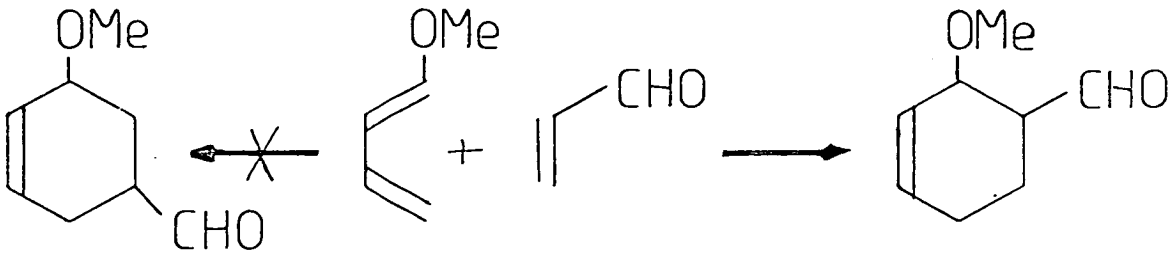


(b)

Figure 12

As indicated by Scheme Seventyfive, only arsorane (236) is expected to yield (234) on reaction with two molar equivalents of dimethyl acetylenedicarboxylate. Thus, the triphenylarsonium phenacylide-methyl propiolate adduct obtained in benzene can be assigned the structure (236) (see Schemes Seventyfour and Seventyfive). Hence, the addition of the phenacylide to methyl propiolate cannot be <u>via</u> attack by the acyl oxyanion, since this would be expected to occur at C-3 of the ester, giving (235) (Scheme Seventytwo). Thus, the addition may be a genuine [4+2] cycloaddition reaction (scheme Seventyone; path b). Several corollaries exist for this mode of

reaction. For example, methoxybutadiene (246) yields the 'ortho' adduct (249) rather than the 'meta' adduct (248) upon reaction with acrolein (247)[169].



(248) (246) (247) (249)

Frontier orbital treatment of this condensation is shown in Figure 13, where the size of the circle is roughly in proportion to the size of the coefficients. The circles represent the p orbitals as seen from above the plane. It is known that the important interaction occurs between the HOMO of the diene and the LUMO of the dienophile. The site selectivity exhibited is due to orbitals of comparable size interacting.

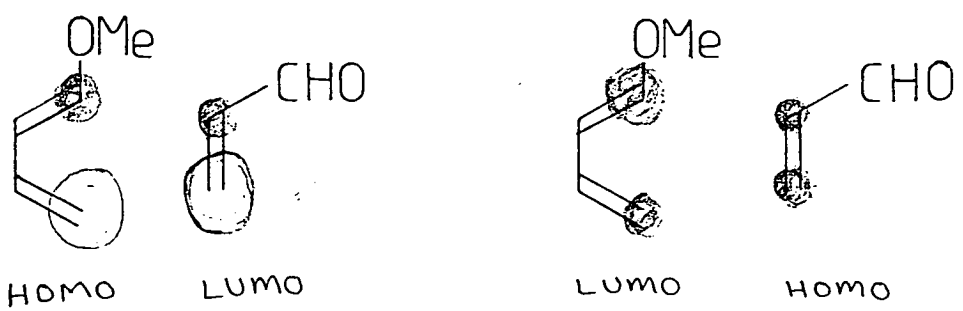


Figure 13

The situation for triphenylarsonium phenacylide is complicated by the involvement of d orbitals rather than p orbitals on the arsenic atom. However, it is

reasonable to assume that the HOMO of the ylide will interact with the LUMO of the ester as shown in Figure 14. Unfortunately, the coefficients of all the orbitals involved are not known.

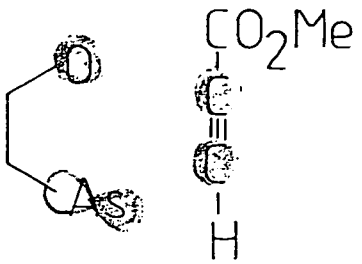
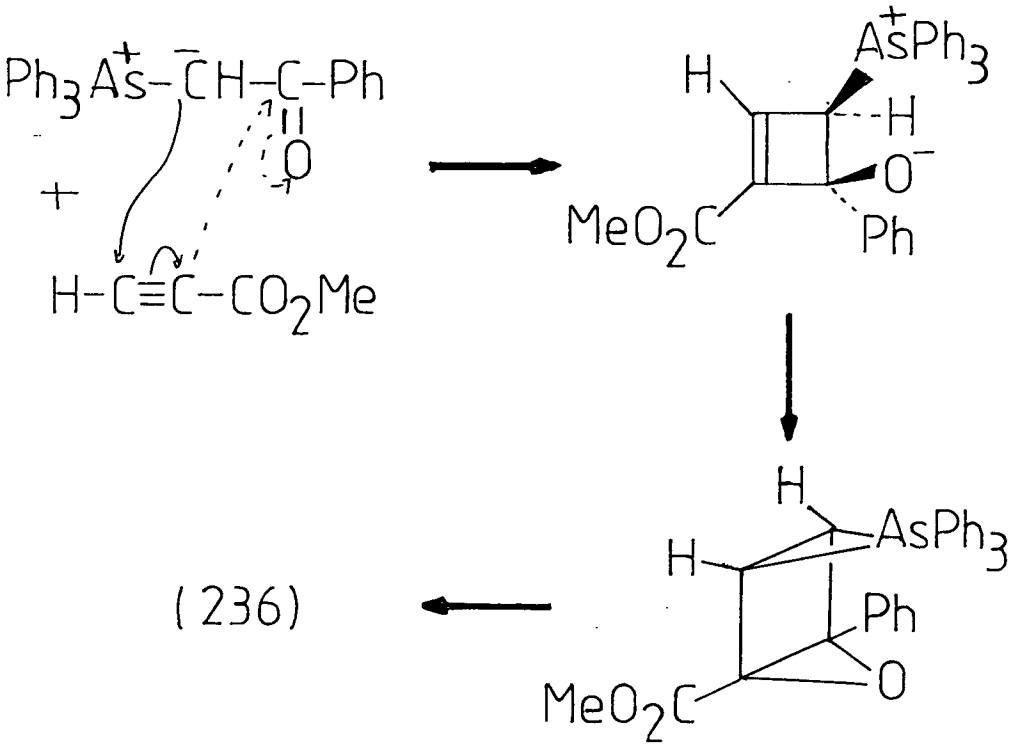


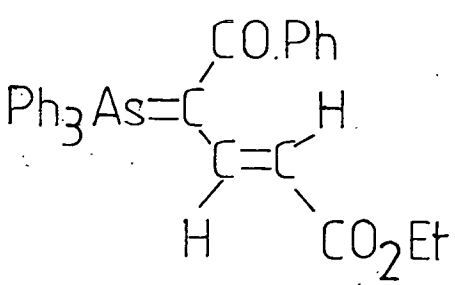
Figure 14

A further mechanism can be postulated to account for the formation of (236) involving an initial [2+2] cycloaddition reaction as shown in Scheme Seventysix. Since thermal [2+2] cycloaddition reactions can not be concerted this addition must be stepwise. With the information at hand, it is not possible to distinguish experimentally between the two proposed routes to (236).

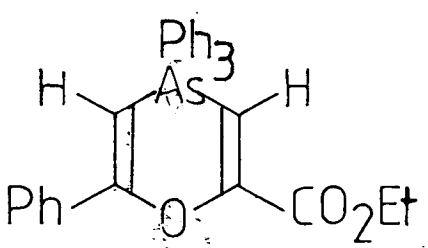


Scheme Seventysix

In the same way, the corresponding reaction of triphenylarsonium phenacylide with ethyl propiolate in ethanol gave ylide (250), while in benzene arsorane (251) was formed.

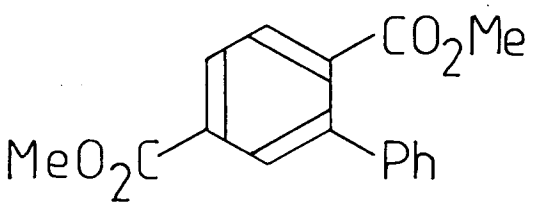


(250)

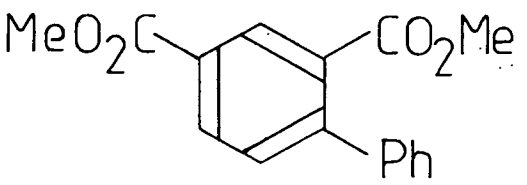


(251)

Interestingly, triphenylarsonium phenacylide reacted with three molar equivalents of methyl propiolate in boiling benzene to afford only the arsorane (236) in good yield, and neither (252) nor (253) could be detected.

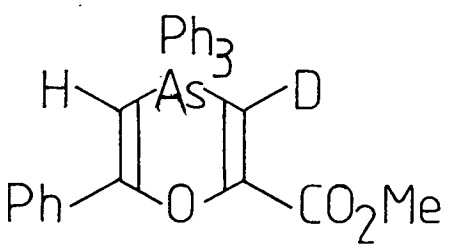


(252)

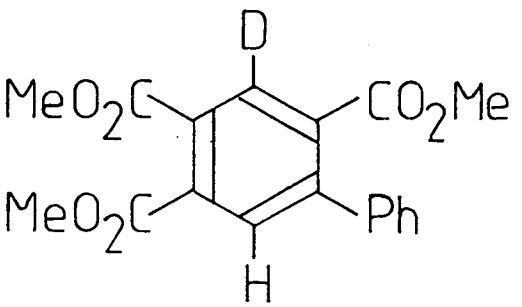


(253)

The reaction of triphenylarsonium phenacylide with d^1-methyl propiolate afforded d^1-labelled arsorane (254), which reacted with dimethyl acetylenedicarboxylate to give the d^1-labelled adduct (255). Accordingly, the ^1H n.m.r. spectrum of (255) showed a diminished singlet at δ8.21 and the singlet at δ7.67 integrated for one proton (Figure 10a). Thus, as expected (Scheme Seventyfive), the acetylenic proton of methyl propiolate lies ortho to two carbomethoxy groups in (234).

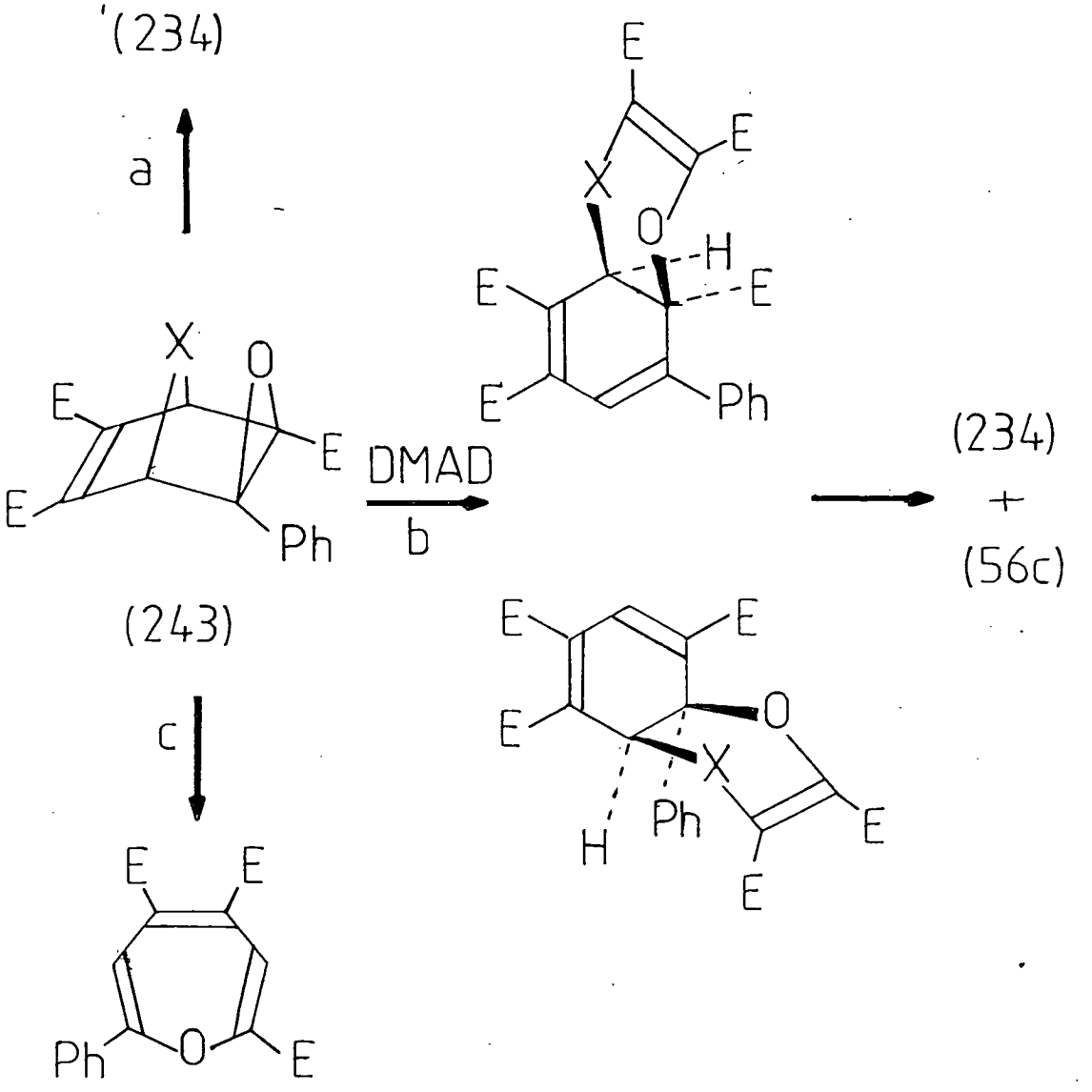


(254)



(255)

From the evidence available it is not possible to elucidate the mechanism for the reaction of the arsorane (236) with dimethyl acetylenedicarboxylate Two pathways can be delineated. In the first triphenylarsine oxide can be lost from a 1:1 adduct of



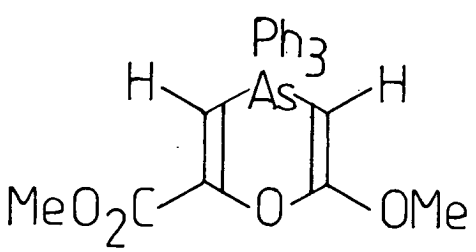
X = $AsPh_3$

E = CO_2Me

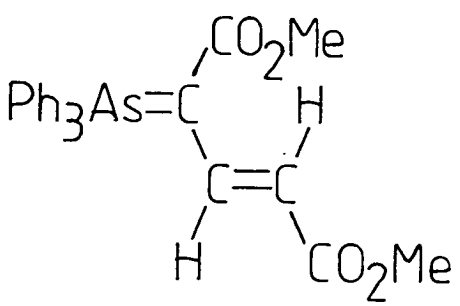
Scheme Seventyseven

arsorane plus dimethyl acetylenedicarboxylate or alternatively, ylide (56c) may be lost from a 1:2 adduct (Scheme Seventyseven). However, the reaction between triphenylarsine oxide and dimethyl acetylenedicarboxylate is in favour of the first pathway; yet it is difficult to see why extrusion of triphenylarsine oxide should be favoured over that of triphenylarsine (Scheme Seventyseven; path c), unless the gain in aromaticity is the determining factor.

An attempt to form an arsorane (i.e. (256)) by reaction of triphenylarsonium carbomethoxymethylide with methyl propiolate in benzene afforded the stabilised arsonium ylide (257), instead*. The trans-geometry about the olefinic double bond was established by the large (14 Hz) coupling between the olefinic protons at δ7.20 and 5.92.



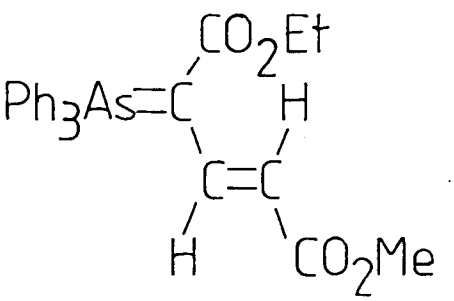
(256)



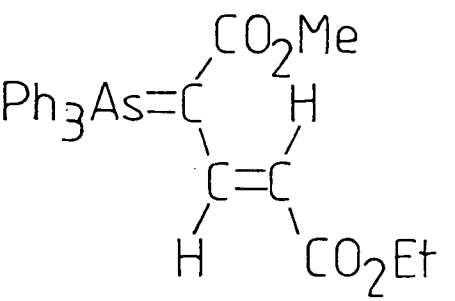
(257)

* The failure to observe (256) is not yet explained. However, subsequent experiments have suggested that the basicity of the arsonium ylide is all important. Thus, it appears that the more basic arsonium keto-ylides afford further ylides, whereas highly stabilised keto-ylides (i.e. low $\nu_{C=O}$) provide arsoranes.

In a similar reaction, triphenylarsonium carbomethoxymethylide and ethyl propiolate afforded a 1:1 adduct in benzene which could be assigned either structure (258) or (259). Again, a trans-geometry about the olefinic double bond was shown by ^{1}H n.m.r. spectroscopy, and the two olefinic doublets (J = 15 Hz) resonated at δ7.22 and 6.02. However, it seems likely that the ylide possesses the structure (258), since in this case there seems to be no advantage to be gained by rearrangement, e.g. greater conjugation.



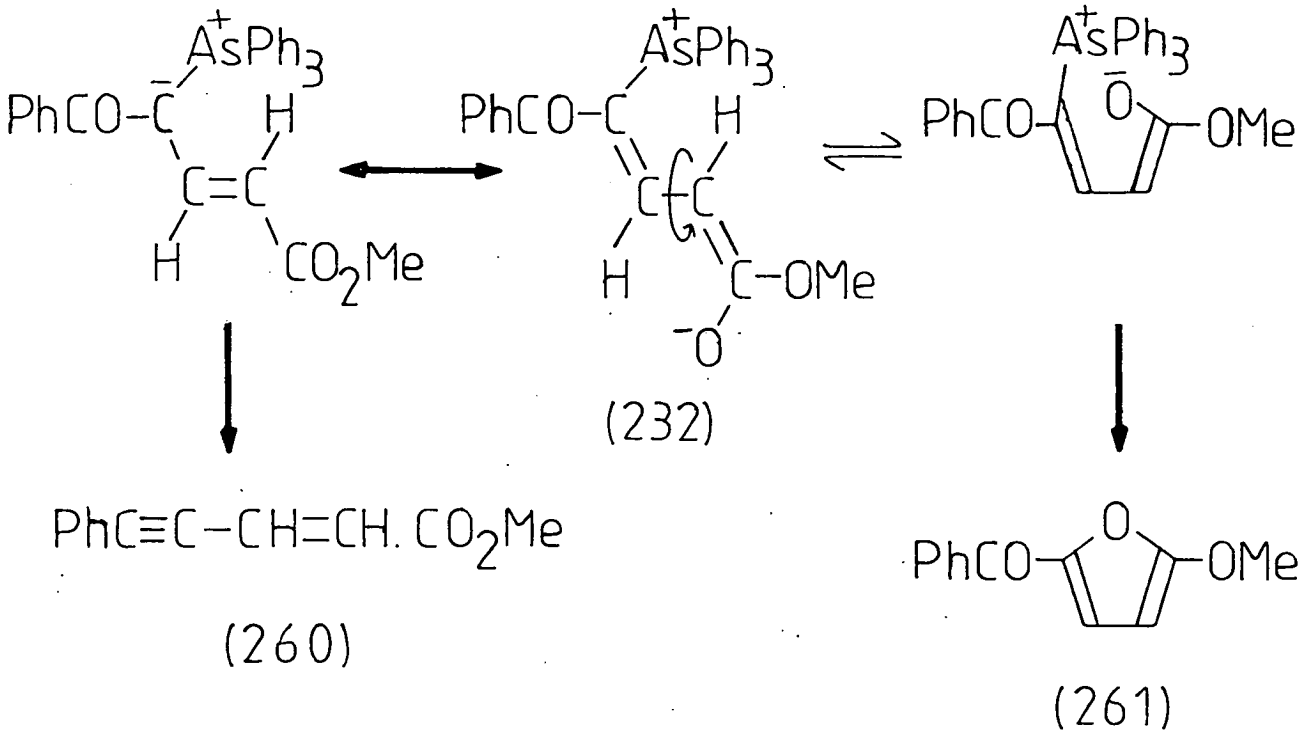
(258)



(259)

2.3.3 Pyrolysis of adducts

Attempts to convert (232) into either the acetylene (260) by loss of triphenylarsine oxide, or the furan (261) by loss of triphenylarsine, were unsuccessful (Scheme Seventyeight). Thus, pyrolysis of (232) under flash vacuum pyrolytic conditions gave a sublimate of triphenylarsine (33%), leaving a residue which could not be separated into its components. The failure to obtain triphenylarsine oxide by extrusion from (232) demonstrates the weakness of the arsenic-oxygen bond compared to the phosphorus-oxygen bond. Under the same conditions, the arsorane adduct (236) extruded triphenylarsine but no other product could be identified.



Scheme Seventyeight

2.3.4 Reaction of triphenylphosphonium phenacylide with methyl propiolate

In contrast to triphenylarsonium phenacylide, triphenylphosphonium phenacylide reacted with methyl propiolate in both methanol and benzene to afford the same 1:1 adduct. The proton n.m.r. spectrum of the adduct showed one ester methoxyl singlet of three protons at δ3.42, a complex multiplet of twenty one protons at δ7.9-7.2, and a single proton as a doublet (J = 16 Hz) at δ4.49 (Figure 15). The i.r. spectrum of the adduct showed two carbonyl stretching frequencies at 1685 and 1580 cm^{-1}. This spectral data is consistent with the structure (262) for the 1:1 adduct but interestingly, no coupling to phosphorus of the proton at δ4.49 could be

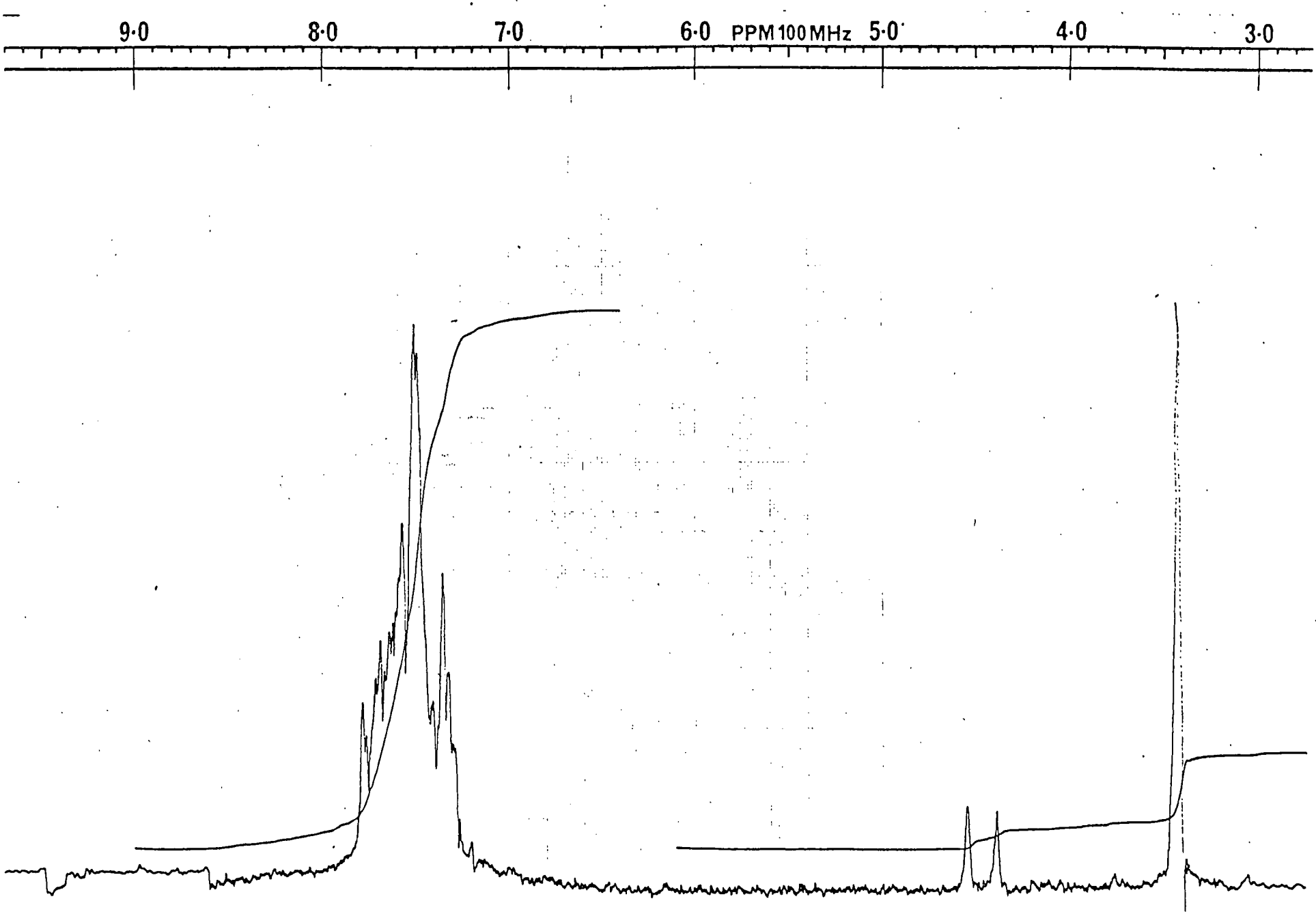
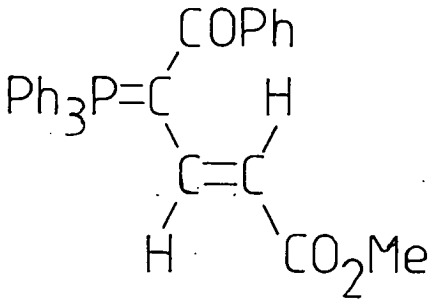
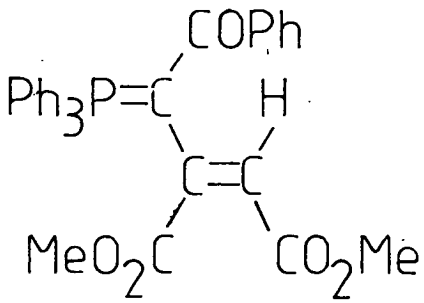


Figure 15. ^{1}H n.m.r. spectrum of (262).

observed, in marked contrast to the 3 Hz coupling reported by Hendrickson and co-workers[88] for ylide (229).



(262)

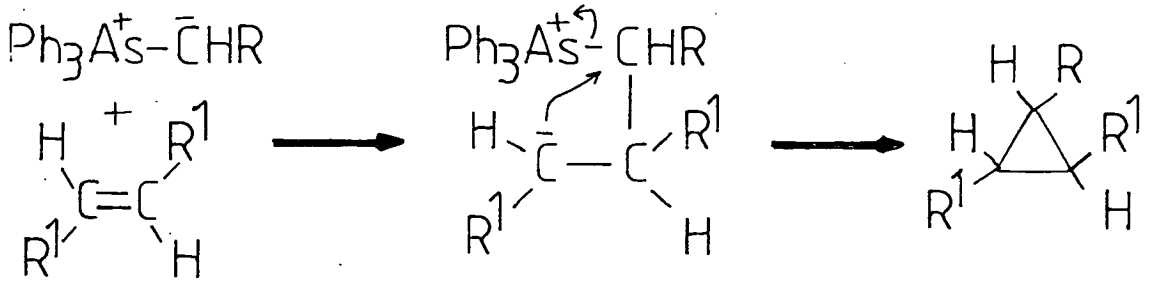


(229)

2.4 Reaction of stabilised arsonium ylides with activated olefins

2.4.1 Introduction

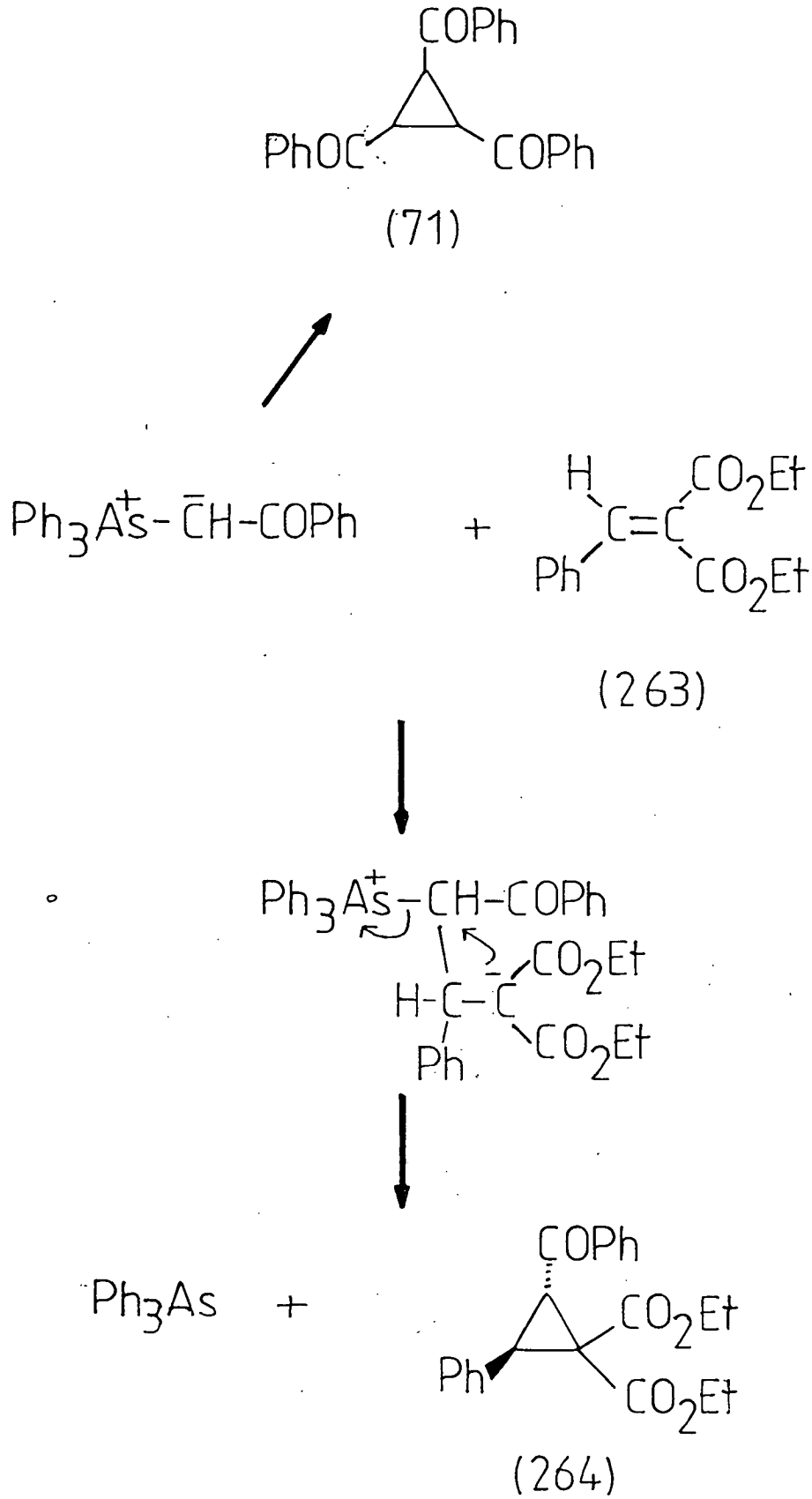
The reaction of arsonium ylides with activated olefins has been reviewed in the Introduction. Unlike the corresponding reaction of phosphonium ylides, that with arsonium ylides has received comparatively little attention. Both Nesmeyanov[82] and Johnson[12], have observed that arsonium ylides react with activated olefins to afford cyclopropanes as shown in Scheme Seventynine. A similar course of reaction has also been observed during the thermoylsis of stabilised arsonium ylides[12,82].



Scheme Seventynine

2.4.2 Reaction with diethyl benzalmalonate

Triphenylarsonium phenacylide formed by treatment of phenacyltriphenylarsonium bromide with sodium ethoxide at 0°C failed to react with diethyl benzalmalonate (263) at room temperature. However, reaction in boiling tetrahydrofuran gave three products after chromatography on alumina. These were identified as triphenylarsine (70%), trans-1,2,3-tribenzoylcyclopropane (71) (7.8%) and



Scheme Eighty

trans-diethyl 2-benzoyl-3-phenylcyclopropan-1,1-dicarboxylate (264) (35%). The cyclopropane derivative (71) is the same product as that obtained[12] from the thermal decomposition of triphenylarsonium phenacylide, while the other cyclopropane derivative (264) is presumably formed by nucleophilic attack of the ylide on the olefin, followed by ejection of triphenylarsine (Scheme Eighty).

The same reaction in a melt at 110°C afforded only two products, namely triphenylarsine (65%) and trans-diethyl 2-benzoyl-3-phenylcyclopropan-1,1-dicarboxylate (44%).

2.4.3 Reaction with diethyl ethoxymethylenemalonate

Reaction of triphenylarsonium carbomethoxymethylide with an excess of diethyl ethoxymethylenemalonate (265) afforded a colourless compound which on the basis of the analytical and spectral evidence was identified as 3-carbomethoxy-1,1-dicarbethoxy-3-triphenylarsenanylprop-1-ene (266). The ^{1}H n.m.r. spectrum of the product is shown in Figure 16. The structurally significant peaks are located at δ7.8-7.1, a sixteen proton complex multiplet assigned to the fifteen phenyl protons and one methine proton, at δ4.03 a four proton quartet (J = 7 Hz) assigned to the coincidental resonances of the four methylene protons, at δ3.41, a three proton singlet assigned to a methoxy group, and δ1.3-1.0, two overlapping three proton triplets (J = 7 Hz) assigned to the six methyl protons.

Triphenylarsonium phenacylide gave an analogous reaction yielding compound (267).

A plausible mechanistic pathway for these reactions is depicted in Scheme Eightyone, and denotes a new synthesis

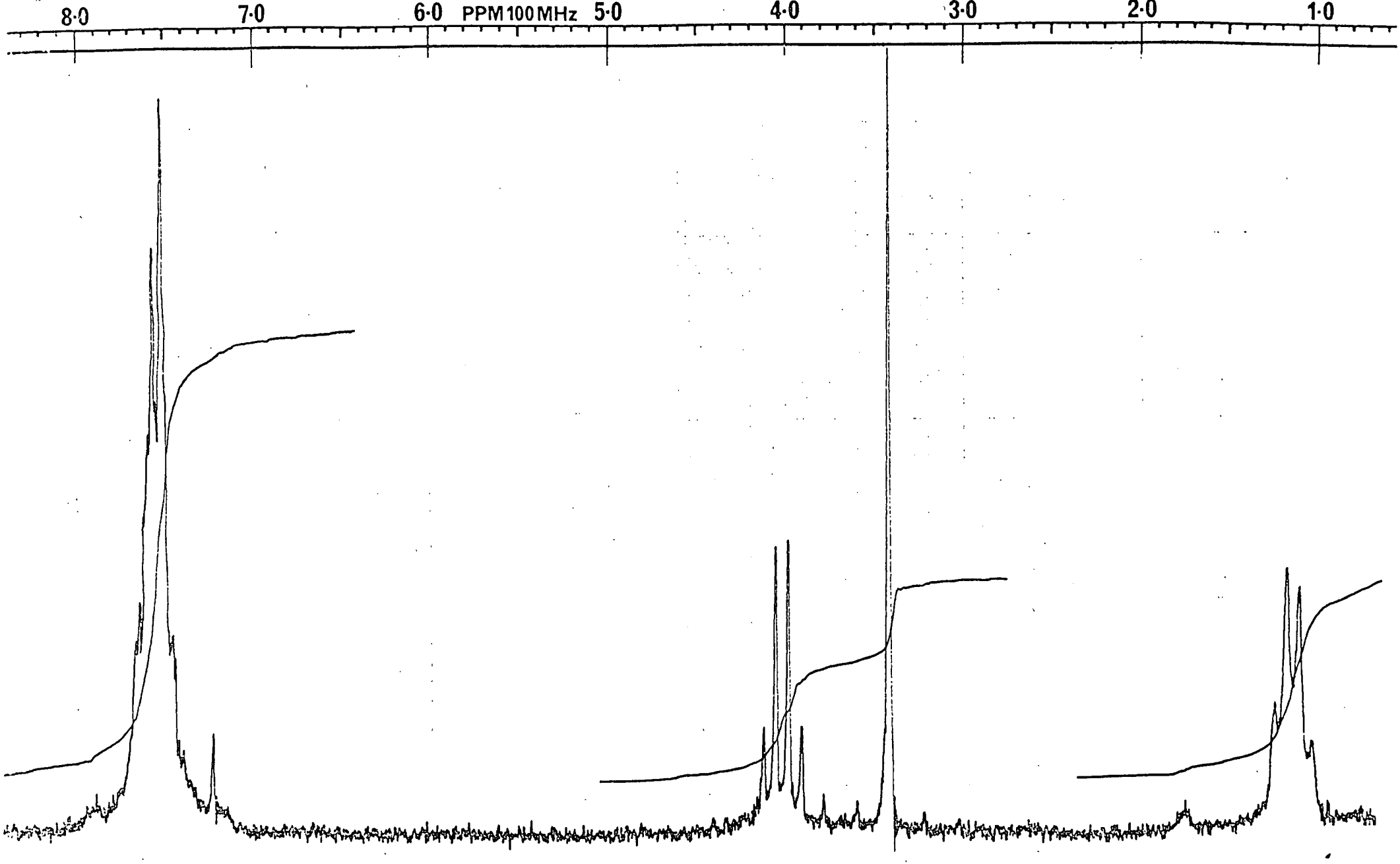
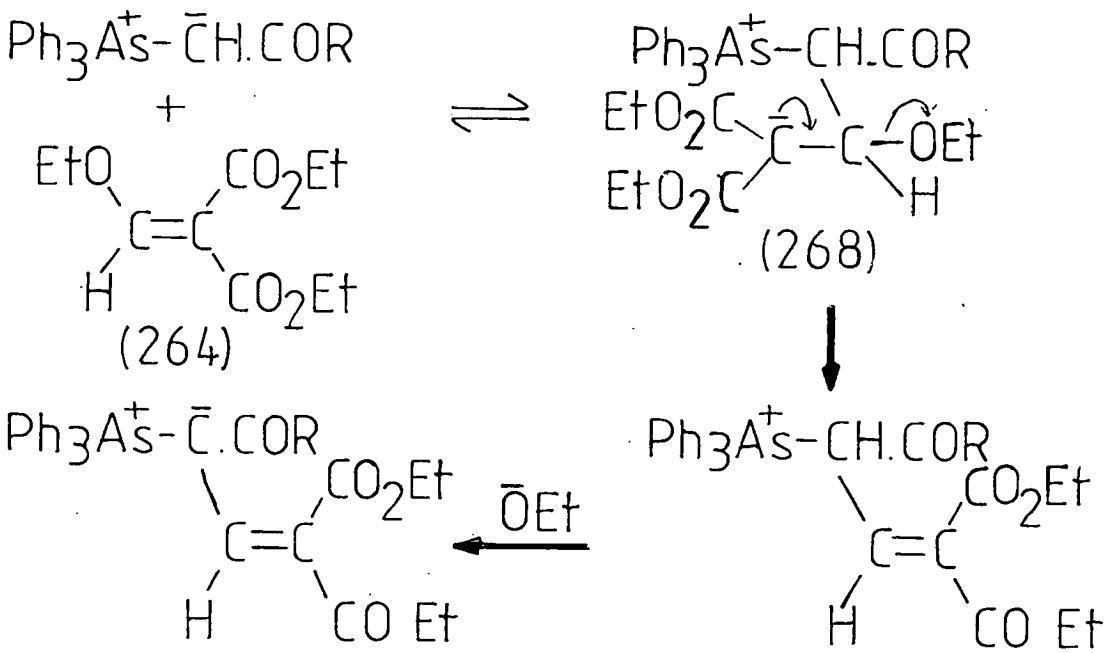


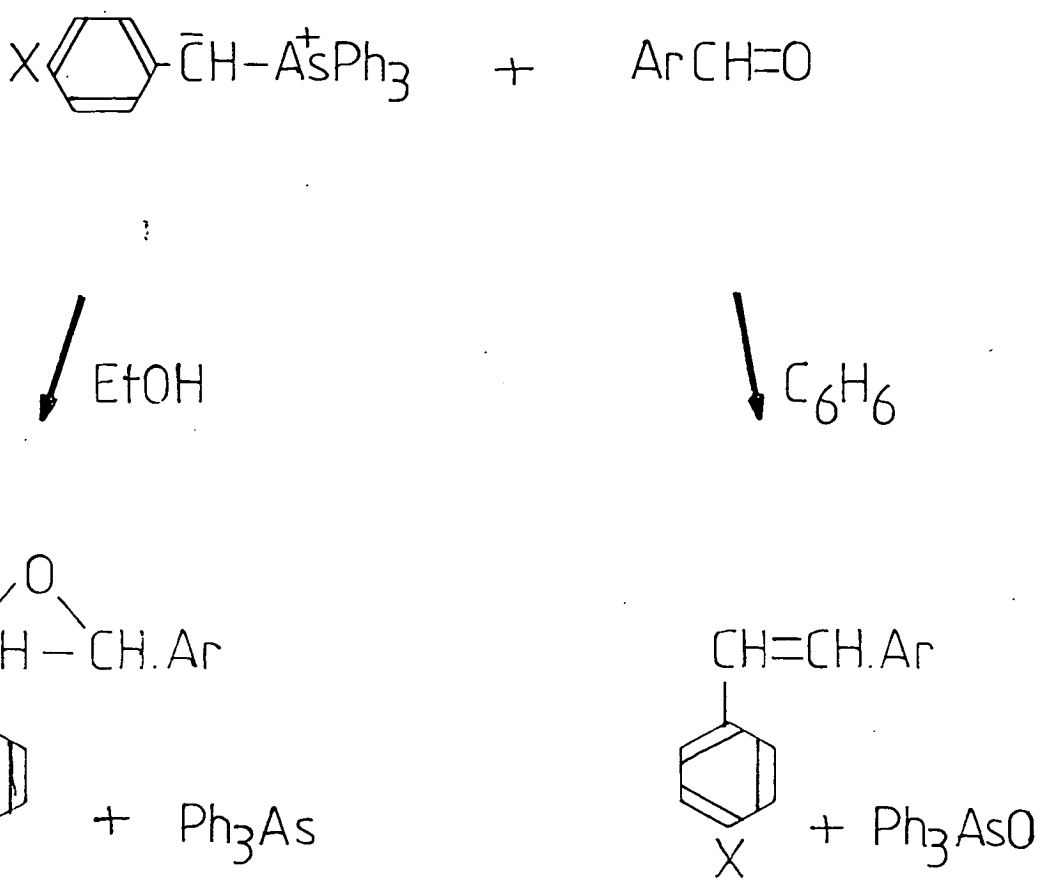
Figure 16. ^{1}H n.m.r. spectrum of (266)

of novel arsonium ylides by a transylation reaction with olefins. It is worth noting that these results accord well with the observations by Trippett for the corresponding reaction of phosphonium ylides[170].
On the other hand, arsonium ylides have been previously found to give cyclopropanes upon addition to the carbon-carbon double bonds[12,82,171]. Presumably, the difference in reaction is due to the presence of a good leaving group alpha to the carbanionic centre in adduct (268). In the absence of such a group, cyclopropanes are obtained.



(266): R = OMe
(267): R = Ph

Scheme Eightyone



X = H; Ar = 4-$NO_2C_6H_4$

X = H; Ar = 4-$OCH_3C_6H_4$

X = 4-Cl; Ar = 4-$NO_2C_6H_4$

X = H; Ar = 4-$N(CH_3)_2C_6H_4$

X = H; Ar = 4-$CH_3C_6H_4$

X = 4-Cl; Ar = 4-$NO_2C_6H_4$

X = 4-Cl; Ar = 4-ClC_6H_4

X = 4-Cl; Ar = 4-$OCH_3C_6H_4$

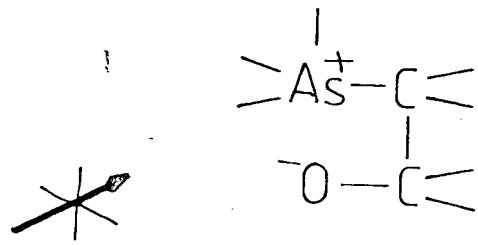
Scheme Eightytwo

2.5 Reaction of ethyldiphenylarsonium benzylide with benzaldehyde

The solvent dependence of the product distribution of the reaction between arsonium ylides and carbonyl compounds has received scant attention. Whilst earlier workers have established that the reaction of arsonium ylides with carbonyl compounds can give rise to either olefins[11,12,19,115,116] or epoxides[125], or a mixture of both[9,10], no study of the effect of solvent on the course of the reaction has been reported apart from that of Tewari[125] involving semi-stabilised ylides. The latter afforded epoxides in ethanol, a polar protic solvent, but olefins in benzene, a non-polar aprotic solvent (Scheme Eightytwo). The usefulness of Tewari's results are undermined by the fact that the study involved only two solvents, the nature of which differed markedly.

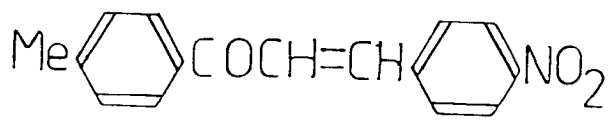
In the only other study to date, Froyen[21] showed that the reaction of stabilised arsonium ylides with p-nitrobenzaldehyde in a variety of solvents (DME, DMSO, methanol, benzene) afforded only olefins, and that the solvent polarity had little influence on the rate of reaction (c.f. methanol) (Table 9). As a result, Froyen proposed that the betaine (269) played little, if any, part in the reaction, and that the reaction proceeded directly *via* a 4-centred cyclic intermediate (270) which eliminates arsine oxide. The strong increase in rate observed in methanol as compared with benzene was tentatively attributed to the hydrogen bonding ability of methanol, and not primarily to the higher polarity.

Table 9. Kinetics of formation of olefin (271)

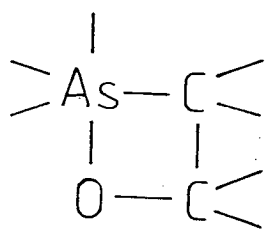


(269)

+



(271)

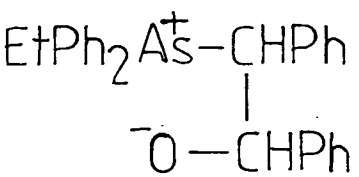


(270)

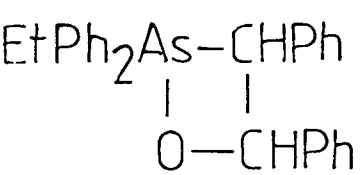
rate constant/ $\ell\ mol^{-1}\ s^{-1}$	solvent*	reaction temperature/^{o}C
5.70±0.05	C_6H_6	25.0
4.50±0.05	C_6H_6	17.2
7.40±0.05	C_6H_6	35.0
1.20±0.05	DMF	25.0
2.70±0.02	DMSO	25.0

*Reaction in methanol is faster, but measurements were not obtained as the ylide is too unstable in this solvent.

In view of the delicate balance between the formation of either olefin or epoxide in the case of semi-stabilised arsonium ylides it seemed worthwhile to make a comparative study of the course of their reactions with aldehydes in solvents of slightly varying polarity. From a mechanistic viewpoint such a study is preferable since the solvent effects, if any, would be expected to involve gradual, yet observable, changes in the product composition. Table 10 shows the product distribution obtained from a study of the reaction of ethyldiphenylarsonium benzylide (272) with benzaldehyde in four solvents - benzene, THF, DME, ether. As the results indicate, the epoxide/olefin ratio increases with increasing solvent polarity (ether < THF < DME). This behaviour presumably reflects the different natures of the two possible reaction paths. (Jackman and Lange[172] have classified these solvents as 'weakly polar solvents which can, however, solvate cations'.) Thus, in the absence of a stabilising polar solvent the betaine (273) at once forms an arsorane (274) which collapses to an olefin, whereas the betaine is stabilised by the more polar solvent and the competing pathway, leading to epoxide, is then promoted.

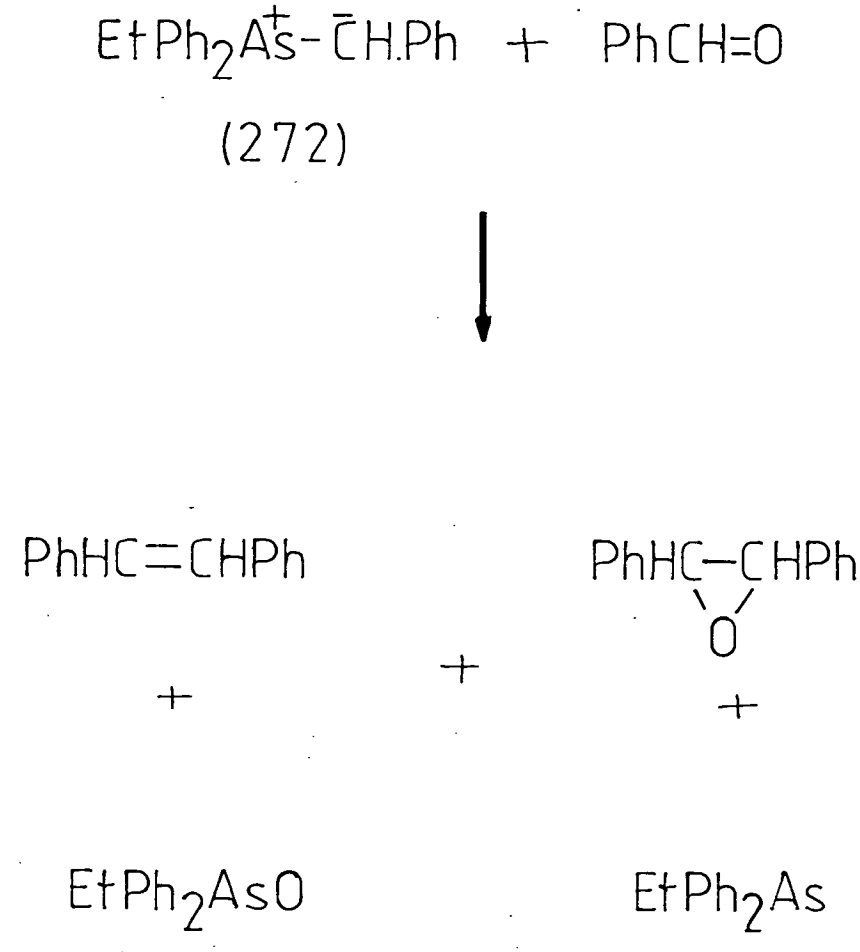


(273)



(274)

Table 10 Epoxide/olefin* ratio for reaction of ylide (272) with benzaldehyde



	Benzene	DME	THF	ether
ratio	6.97	3.80	1.54	1.40

*average values

The formation of predominantly epoxide in benzene is surprising, especially when compared with the results of Tewari[125] and the above arguments. Perhaps the difference lies in the nature of the arsine moiety of the ylide and, clearly, further work is necessary in order to shed light on this anomalous finding.

Abbreviations

b.p.	boiling point
m.p.	melting point
t.l.c.	thin layer chromatography
g.l.c.	gas liquid chromatography
n.m.r.	nuclear magnetic resonance
i.r.	infrared
u.v.	ultraviolet
dec.	decomposed
DME	1,2-dimethoxyethane
THF	tetrahydrofuran
DMSO	dimethylsulphoxide
DMF	dimethylformamide

Instrumentation and General Techniques

Gravity column chromatography: The alumina used was Laporte Industries Ltd., activated aluminium oxide, type H (Brockman activity = 1) unless otherwise stated.

Thin layer chromatography: Thin layer chromatograms were obtained on 0.3 mm layers of alumina (Merck, aluminium oxide G, type 60/E) or silica gel (Merck, silica gel G, type 60) containing fluorescent indicator. Components in the developed chromatograms were detected by observing the plate under u.v. light, or by their reaction with iodine.

Nuclear magnetic resonance spectroscopy: 60 MHz proton magnetic resonance spectra were recorded on a Varian EM360 spectrometer, at a probe temperature of 33°C. 100 MHz spectra were obtained using a Varian HA100 instrument, at a probe temperature of 28°C, unless otherwise stated. Decoupling and variable temperature experiments, when required, were also carried out on this machine. Chemical shifts are recorded as delta (δ) values in parts per million from tetramethylsilane (δ = 0.00), which was used as an internal reference. Spectra were recorded on 10-15% w/v solutions in deuteriochloroform, unless otherwise stated.

Where necessary spectra were recorded on a Bruker WH360 spectrometer.

Carbon 13 n.m.r. spectra were obtained on a Varian CFT20 spectrometer, using the pulse and Fourier

transform technique, at 20 MHz. Spectra were recorded at temperatures between 28 and 36°C. The deuterium signal from the solvent ($CDCl_3$ in all cases) was used for field frequency lock, and chemical shift values were recorded in parts per million from TMS.

For all forms of n.m.r. spectroscopy used, positive δ values are to low field relative to the reference.

Infrared spectroscopy: I.r. spectra were recorded on a Perkin Elmer 157G Grating Infrared Spectrometer. Samples were examined as nujol mulls unless otherwise stated.

Mass spectrometry: Mass spectra and accurate mass measurements were obtained using an A.E.I. MS-902 double focussing mass spectrometer.

Elemental analyses: Microanalyses were carried out on a Perkin Elmer 240 Elemental Analyser by Mr. J. Grunbaum, University of Edinburgh.

Melting points: The melting points of all new compounds were determined using a Kofler hot stage instrument and are uncorrected.

Solvents: Tetrahydrofuran and dimethoxyethane were distilled under nitrogen from calcium hydride and stored over molecular sieve Type 4A. Sodium dried diethyl ether was distilled under nitrogen from lithium aluminium hydride and stored over molecular sieve Type 4A. Sodium dried benzene was distilled under nitrogen from fresh sodium wire and stored over sodium wire.

"Super-dry" methanol and ethanol were prepared as described by Vogel (method 1).

Petrol refers to the fraction b.p. 40-60°C unless otherwise stated.

All other solvents were distilled and stored over molecular sieve where appropriate.

Gas chromatography

Gas chromatography was carried out using a Pye Series 104 Chromatograph with a flame ionisation detector and nitrogen carrier gas. Samples in a chloroform solution were analysed with a 2% carbowax (20 M on celite 85-100) column at 170°C using a flow rate of approximately 60 cc of N_2 per minute.

Before commencing each analysis all connections were tested with soap solution as even small leaks around the septum or at the column connections lead to irreproducible results. The air flow was checked before and after each run for any appreciable deviations since the response of flame ionisation detectors can be variable and inconsistent with inadequate air supply. In gc analysis the area of a peak is proportional to the amount of compound injected but the proportionality constant (response factor) varies from compound to compound, i.e.

$W_X = K_X.A_X$ where A_X = area of peak produced by injecting Wxg of compound X. The response factor K_X is specific for compound X and a given set of operating conditions. The quantitative analysis of the product

mixtures (see 3.13) was achieved by the internal-standard procedure. The chosen internal standard (M) must give a peak in a clear part of the chromatogram.

The calibration mixtures (see 3.13) were prepared when required and not retained for any length of time. For each calibration mixture at least three samples were injected until concordant ($\pm$3%) peak area ratios A_X/A_M and A_Y/A_M were obtained. If a calibration mixture contained W_X, W_Y and W_M grammes of X, Y and M, respectively and gave corresponding peak areas of A_X, A_Y, A_M then $W_X/W_M = K_X/K_M.A_X/A_M$ where K_X/K_M is known as the correction factor K_X. Therefore

$$K_X = W_X A_M / W_M A_X$$

Thus K_X and K_Y were determined for both calibration mixtures and if they were not consistent further calibration mixtures were used until consistency was obtained. The product mixture containing a known amount of internal standard (W_{IS}) was injected onto the column until concordant ($\pm$3%) peak area ratios were obtained. If the compounds X, Y and the internal standard give peak areas A_X^1, A_Y^1, A_{IS}, then the weight of X present in the product mixture is given by

$$X = K_X W_{IS} A_X^1 / A_{IS}$$

and similarly for component Y.

The method used to measure peak areas was a manual one. The peak height was multiplied by the peak width at half peak height, i.e. area = h x $w_{\frac{1}{2}}$.

The separating efficiency of a column can be expressed as the total number of theoretical plates (N) which can be derived from chromatograms using the expression

$$N = 5.54 \, (O_X/W_{\frac{1}{2}})^2$$

where $W_{\frac{1}{2}}$ = peak width at half height, and O_X = distance from injection point to peak maximum. A conventionally packed column should achieve plate heights of 0.05 - 0.02 cm where the theoretical plate height (H) is found by dividing the column length by N.

3.1 Preparation of arsines

3.1.1 Chlorodiphenylarsine

Triphenylarsine (18.63 g; 60.9 mmol) and arsenic trichloride (2.73 g; 15.1 mmol) were heated together for 3.5 hr in a sealed tube at 260°C. The reaction mixture was distilled twice under reduced pressure to give chlorodiphenylarsine (10.25 g; 38.7 mmol), b.p. 134-142°C at 0.8 mmHg (lit.,[173] 172-175°C at 11 mmHg) as a colourless liquid.

3.1.2 Ethyldiphenylarsine

The Grignard reagent of ethyl bromide was prepared from dry magnesium turnings (1.4 g; 58.3 mmol) and ethyl bromide (4.7 g; 43.1 mmol) in sodium dried ether (50 ml). The chlorodiphenylarsine (10.1 g; 38.2 mmol) was added dropwise to the solution of Grignard reagent over a period of 30 min. The reaction mixture was heated under reflux for 2 hr, cooled and decomposed with dilute sulphuric acid. The ethereal layer was removed, the aqueous portion washed with ether (3x50 ml), and the combined ether portions dried over anhydrous magnesium sulphate. The ether was removed *in vacuo* and the remaining oil (9.3 g) distilled under reduced pressure to give ethyldiphenylarsine (6.96 g; 26.9 mmol), b.p. 114-118°C at 0.4 mmHg (lit.,[174] 151-152°C at 2 mmHg) as a colourless oil.

3.1.3 Tris(p-chlorophenyl)arsine

Tris(*p*-chlorophenyl)arsine was prepared by a modification of the procedure described by Hanby and Waters[175]. *p*-Chloroaniline was diazotized in hydrochloric

acid and the zinc chloride double salt was precipitated by the addition of aqueous zinc chloride solution at 0°C. The dried double salt, arsenic trichloride and zinc dust were stirred in dry acetone overnight. The reaction mixture was filtered, the filtrate evaporated, and the residual acetone removed by steam distillation. Dilute hydrochloric acid precipitated a brown solid which was extracted into dichloromethane. Column chromatography on alumina afforded tris(p-chlorophenyl)arsine (15.8%), m.p. 106-108°C (lit.,[175] 75°C); p^+: 412, 410, 408, as colourless crystals.

3.1.4 Tris(p-dimethylaminophenyl)arsine

p-Bromo-N,N-dimethylaniline (20.35 g; 102 mmol) in anhydrous ether (75 ml) was added dropwise with vigorous stirring to freshly cut lithium (1.65 g; 238 mmol) in ether (35 ml). After the initial reaction had ceased, the mixture was boiled for 1 hr (90% reaction was assumed The ether solution was cooled to -20°C and arsenic trichloride (5.75 g; 54 mmol) in ether (20 ml) was added dropwise with stirring. The suspension stood for 1 hr and was then heated under reflux for a further 2 hr. The ether was removed in vacuo and the solid decomposed with methanol (20 ml) and then water (100 ml). The solid (12.49 g; 28.7 mmol) was filtered and recrystallised from ethanol to give colourless crystals of tris(p-dimethylaminophenyl)arsine, m.p. 229-231°C dec. (lit.,[176] 240-242°C).

3.2 Preparation of arsonium salts

3.2.1 Benzylethyldiphenylarsonium bromide

Ethyldiphenylarsine (6.51 g; 25.2 mmol) and benzyl

bromide (5.74 g; 33.9 mmol) were heated under reflux in benzene (50 ml) for 24 hr. The reaction mixture was evaporated *in vacuo* and the remaining oil triturated with ether to give the title compound as a white solid (7 g; 16.3 mmol) which was recrystallised twice from ethanol/ether as colourless crystals, m.p. 192-194°C (lit.,[177] 191-192°C).

3.2.2 Benzyltriphenylarsonium bromide

Triphenylarsine (3.08 g; 100 mmol) and benzylbromide (17.5 g; 100 mmol) were heated together in ethanol (150 ml) under reflux for 12 hr. Then ether (100 ml) was added to the solution which was then allowed to cool to room temperature. The arsonium salt was precipitated as colourless crystals (27.1 g; 56.8 mmol), m.p. 169-170°C (from ethanol/ether) (lit.,[177] 176°C).

3.2.3 p-Nitrobenzyltriphenylarsonium bromide

Triphenylarsine (15.3 g; 50 mmol) and p-nitrobenzylbromide (10.8 g; 50 mmol) were heated together in ethanol (100 ml) under reflux for 4 hr. Then three quarters of the ethanol was distilled off and 60-80 petrol ether added to precipitate the salt (17.1 g; 32.7 mmol) which was recrystallised twice from chloroform/benzene as colourless crystals, m.p. 154-155°C (lit.,[31] 151-152°C).

3.2.4 Tris(p-chlorophenyl)-p-nitrobenzylarsonium tetrafluoroborate

This compound was prepared by the method described by Dwyer[142] for the preparation of tris(p-chlorophenyl)benzylarsonium tetrafluoroborate. A mixture of p-nitrobenzylbromide

(8.64 g; 40 mmol) and tris(p-chlorophenyl)arsine (4 g; 9.69 mmol) in 1,2-dichloroethane (16 ml) was stirred at room temperature under a nitrogen atmosphere for 3 hr. Then a suspension of silver tetrafluoroborate (1.9 g; 9.69 mmol) in 1,2-dichloroethane (15 ml) was added dropwise with stirring. Almost immediately a precipitate was observed. The reaction vessel was wrapped in aluminium foil for four days, after which time the solid was filtered off and the filtrate evaporated *in vacuo* to afford an oily solid. Recrystallisation of the oil from dichloromethane/ether gave *p*-nitrobenzylbromide (4.14 g; 48%), m.p. 93-94°C (lit.,[178] 98°C). The mother liquors were evaporated to give another oil which upon trituration with ether afforded tris(p-chlorophenyl)-p-nitrobenzylarsonium tetrafluoroborate as yellow needles, m.p. 223-225°C (from dichloromethane/ether).

Found: C, 47.66; H, 2.85; N, 2.0%

$C_{25}H_{18}AsBCl_3F_4NO_2$ requires: C, 47.47; H, 2.87; N, 2.21%

N.m.r. δ_H 7.85 (2H, *d*, J = 7.8 Hz, aromatic protons ortho to NO_2), 7.7-7.4 (15H, *c*, phenyl protons), 7.26 (2H, *d*, J = 7.8 Hz, aromatic protons meta to NO_2), 4.98 (2H, *s*, CH_2), total integration correct.

I.r. ν_{max} 1518 (NO_2), 1075 (BF_4) cm^{-1}.

3.2.5 *p*-Bromobenzyltriphenylarsonium bromide

Triphenylarsine (8.18 g; 26.7 mmol) and *p*-bromobenzylbromide (7.5 g; 30.0 mmol) were heated under reflux in anhydrous benzene (45 ml) under nitrogen for 6 hr. The solvent was removed *in vacuo* and the residual oil recrystallised from chloroform/hexane to give *p*-bromobenzyltriphenylarsonium bromide (6.64 g; 11.9 mmol) as colourless rhombic crystals, m.p. 159-160°C (lit.,[33] 182-184°C).

3.2.6 Carbomethoxymethyltriphenylarsonium bromide

Methyl bromoacetate (20 g; 130 mmol) and triphenylarsine (40 g; 130 mmol) were stirred together for 1 hr at room temperature, then benzene (20 ml) was added and the stirring continued for three days. Then the reaction mixture was filtered and the precipitate washed with ether to give carbomethoxymethyltriphenylarsonium bromide (28 g; 61 mmol) as colourless crystals, m.p. 177-178°C (lit.,[179] 169-170°C).

3.2.7 Phenacyltriphenylarsonium bromide

Phenacylbromide (5.16 g; 25 mmol) and triphenylarsine (6.1 g; 20 mmol) dissolved in benzene (30 ml) were heated under reflux for 4 hr. The reaction mixture was filtered cold to give phenacyltriphenylarsonium bromide (5.42 g; 10.7 mmol), recrystallised once from chloroform/benzene as colourless crystals, m.p. 180-181°C (lit.,[62] 186°C).

3.2.8 Isopropyltriphenylarsonium triiodide

An attempt to prepare the iodide analogue of the title compound gave only the title compound in poor yield as the sole product. Triphenylarsine (15 g; 49 mmol) and 2-iodopropane (11 g; 65 mmol) were heated together in a sealed tube for 66 hr at 100°C. The reaction mixture was poured into ether (50 ml) and triturated to give the title compound as a brown solid (1.22 g; 1.67 mmol). No more salt was obtained by the distillation of the filtrate. Recrystallisation of the brown solid from chloroform/hexane gave isopropyltriphenylarsonium triiodide as red needles, m.p. 164.5-165.5°C.

Found: C, 34.28; H, 2.85%

$C_{21}H_{22}AsI_3$ requires: C, 34.55; H, 3.03%.

N.m.r. ($CDCl_3$ - WH 360) δ_H 7.84-7.68 (15H, c, phenyl protons), 4.357 (1H, h, J = 7.5 Hz, CH), 1.605 (6H, d, J = 7.5 Hz, CH_3), total integration correct.

I.r. ν_{max} 2900, 1577, 1440, 1080, 995, 747, 733, 685 cm^{-1}.

The title compound was decolourised by sodium thiosulphate in a solution in dichloromethane.

3.2.9 Isopropyltriphenylarsonium tetrafluoroborate

Attempts to prepare the bromide analogue of the title compound by heating a mixture of triphenylarsine and 2-bromopropane in a sealed tube (48 hr; 110°C) or by heating the mixture in toluene for several hours did not yield the desired product. The tetrafluoroborate salt was prepared by Dwyer's method[142]. Triphenylarsine (6.12 g; 20 mmol) and 2-bromopropane (10 ml; 13.1 g; 106 mmol) were stirred together at room temperature under a nitrogen atmosphere for 1 hr. Then silver tetrafluoroborate (3.9 g; 20 mmol) in 1,2-dichloroethane (20 ml) was added dropwise with stirring. Immediately a precipitate was observed. The reaction vessel was wrapped in aluminium foil for 24 hr. The reaction mixture was then filtered and the filtrate evaporated *in vacuo* to give an oil which on trituration gave a white solid (2.78 g; 6.4 mmol). Recrystallisation from dichloromethane/ether gave isopropyltriphenylarsonium tetrafluoroborate as fibrous colourless needles, m.p. 220-221°C.

Found: C, 57.47; H, 4.58%

$C_{21}H_{22}AsBF_4$ requires: C, 57.83; H, 5.08%

N.m.r. δ_H 7.9-7.7 (15H, brs, phenyl protons), 4.41 (1H, h, J = 7.2 Hz, CH), 1.61 (6H, d, J = 7.2 Hz, CH_3), total integral correct.

I.r. ν_{max} 2930, 2920, 1460, 1340, 1315, 1155, 1122, 1085, 960, 937, 920, 905, 755, 748, 690 cm^{-1}.

3.2.10 Benzyltris(p-dimethylaminophenyl)arsonium bromide

Tris(p-dimethylaminophenyl)arsine (4.48 g; 10.3 mmol) and benzylbromide (2.87 g; 16.8 mmol) were heated under reflux in benzene (120 ml) with stirring for 3 hr. The cooled reaction mixture was filtered to afford a grey solid (1.58 g). The filtrate was reduced to a third volume to afford further product (1.78 g; 5.5 mmol overall). Recrystallisation from ethanol/ether gave the arsonium salt as pale grey crystals, m.p. 232-234°C (lit.,[177] 218°C).

3.3 Preparation of arsonium ylides

Triphenylarsonium phenacylide and triphenylarsonium carbomethoxymethylide were prepared by treatment of their hydrobromide salts in benzene at room temperature with excess sodium hydride. The reaction mixture was filtered after 48 hr and the filtrate evaporated in vacuo to afford a pale yellow solid. Recrystallisation from benzene/petrol gave the ylide as colourless crystals.

3.3.1 Phenacylide m.p. 178.5-179°C (lit.,[12] 170°C) (99%).

3.3.2 Carbomethoxymethylide m.p. 165-166°C (lit.,[21] 160°C) (100%).

3.4 Preparation of 3-isothiazolones

3.4.1 N-Ethyl-3-isothiazolone

This compound was prepared by the method of Crow and Leonard[180] by the reaction of cis-N-ethyl-3-thiocyanoacrylamide with ferrous sulphate in basic aqueous solution. Continuous extraction into ether followed by sublimation (50°C; 0.5 mmHg) gave colourless crystals of N-ethyl-3-isothiazolone (60%), m.p. 57-58°C (lit.,[180] 61-62°C).

3.4.2 3-Isothiazolone

This compound was made in collaboration with C.J. McGregor from cis-3-thiocyanoacrylamide by the method used for N-ethyl-3-isothiazolone

3.4.3 N-Carbomethoxy-3-isothiazolone

This compound was made in collaboration with C.J. McGregor by the method of Chan[134] from the reaction of 3-isothiazolone with methyl chloroformate.

3.5 Preparation of diazo compounds

3.5.1 Ethyl diazoacetate

Ethyl diazoacetate was prepared by a slight modification of the method described by Hinckinbottom[181]. Glycine ester hydrochloride (50 g; 0.34 mol) and finely powdered sodium nitrite (37.5 g; 0.54 mol) were added to water (100 ml) in a 500 ml separating funnel. The mixture was shaken until the temperature had fallen to 0°C, when ether was added and the whole mixture shaken thoroughly for 1 min. Then the lower aqueous layer was run into a flask cooled in ice and the ethereal layer transferred to a dry flask. The aqueous

layer was washed with ether (25 ml) and the procedure repeated eight times, but with the solution being acidified with 10% sulphuric acid each time before shaking. The combined ether fractions were shaken with aqueous saturated sodium carbonate solution (3x25 ml), dried over anhydrous calcium chloride and the ether removed in vacuo. Distillation of the resulting oil gave ethyl diazoacetate (17.21 g; 0.15 mol) as a yellow oil, b.p. 75°C at 50 mmHg (lit.[181] 86°C at 88 mmHg).

3.5.2 Diazo-5,5-dimethylcyclohexan-1,3-dione

This compound was prepared by the method described by Regitz and Stadler[182]. Dimedone was added to a cooled solution of triethylamine in ethanol. To this stirred solution was added tosyl azide all at once. The solution was stirred for 25 min at 0°C, during which time crystals fell out of solution. Filtration afforded pale yellow fluffy needles of the diazo compound, m.p. 102-103°C (lit.,[182] 108°C). The ether layer was washed with alkaline solution, dried over anhydrous magnesium sulphate, and then reduced to a tenth volume to afford a further crop of crystals, m.p. 102-103°C (42% overall).

Meldrum's diazo (49%), 92.5-93.5°C (lit.,[182] 94°C) was also prepared by this method. Both compounds showed diazo absorptions in their infrared spectra.

3.5.3 Diazoacetylacetone

This compound was prepared by the method described by Regitz[183]. To acetylacetone and piperidine in dry dichloromethane was added tosyl azide with stirring at 0°C.

The reaction mixture was stirred at 0°C for a further 30 min, washed with potassium hydroxide solution and then with water. The organic layer was dried over sodium sulphate and the solvent removed *in vacuo* to afford the diazo compound (41%) as an oil which was suitable for use.

Diazo ethylacetoacetate (64%) was also prepared by this method. Both compounds showed diazo absorptions in their infrared spectra.

3.5.4 Dimethyl diazomalonate

This compound was prepared by the method of Regitz[183] by Dr. J. Brennan.

3.5.5 9-Diazo-10-phenanthrenone

This compound was prepared by Miss E. Henry.

3.5.6 1-Diazo-2,3,4-triphenylcyclopentadiene

This compound was prepared by Dr. I. Gosney.

3.5.7 4,4^{1}-Di-tert-butylphenylbenzoyldiazomethane

This compound was prepared by Miss E. Henry.

3.5.8 2-Diazoacenaphthen-1-one

This compound was prepared by Dr. A. Johnstone.

3.6 Preparation of miscellaneous starting materials

3.6.1 trans-Stilbene oxide

A solution of 85% *m*-chloroperbenzoic acid (2.4 g) in dichloromethane (25 ml) was added slowly to a cooled solution

of trans-stilbene (1.82 g; 10.1 mmol) in dichloromethane (10 ml) and allowed to stand for 5 hr. The reaction mixture was washed with 10% aqueous sodium hydroxide solution (2x20 ml) and then water (2x20 ml). The dichloromethane portion was dried over anhydrous magnesium sulphate and the solvent removed in vacuo at room temperature to leave the epoxide as an oil (1.79 g; 9.1 mmol) which solidified on standing. Two recrystallisations from ethanol gave the epoxide as white fluffy crystals (0.7 g; 3.6 mmol) m.p. 68-69°C (lit.,[184] 68°C).

cis-Stilbene oxide was prepared in the same way by Dr. T.J. Lillie.

3.6.2 Methyl propiolate

Concentrated sulphuric acid (5.7 g) was added with cooling to propiolic acid (19.9 g; 0.284 mol) dissolved in pure methanol (45 ml). The reaction mixture was stirred for two days, and then poured onto iced water and the ester extracted with ether (50 ml, then 2x25 ml). The ethereal layer was washed with saturated aqueous sodium bicarbonate solution, water, dried over anhydrous calcium chloride, then distilled using a fractionating column to afford methyl propiolate (9.96 g; 0.118 mol), b.p. 99.5°C (lit.,[185] 102°C at 742 mmHg).

Ethyl propiolate (45%), b.p. 118°C (lit.,[186] 120°C) was prepared from propiolic acid and ethanol.

Methylbromoacetate (23 g; 0.150 mol), b.p. 60°C at 27 mmHg (lit.,[187] 59-60°C at 20 mmHg), was prepared in the same manner from bromoacetic acid (29 g; 0.208 mol), concentrated sulphuric acid (3 g) and methanol (45 ml). The

ether was removed *in vacuo* prior to the distillation at reduced pressure under nitrogen.

3.6.3 d'-Methyl propiolate

Methyl propiolate was treated with sodium in deuterium oxide overnight. The ester layer was separated, washed with deuterium oxide and then dried over calcium chloride. Filtration gave the deuterated ester. The extent of the deuteration was estimated with the aid of proton n.m.r. spectroscopy.

3.6.4 N-Ethylpropiolamide

This compound was prepared by the method described by Crow and Leonard[180] from methyl propiolate and ethylamine at -80°C. The *N*-ethylpropiolamide was distilled, b.p. 76°C at 1 mmHg (lit.,[180] 74-76°C at 0.8 mmHg), and solidified on standing (71%).

N-Methylpropiolamide (75%), m.p. 87-89°C (lit.,[180] 90-91°C) was prepared in the same manner from methyl propiolate and methylamine.

Propiolamide was prepared in collaboration with C.J. McGregor from methyl propiolate and ammonia.

3.6.5 Diethyl benzalmalonate

Benzaldehyde (10.6 g; 100 mmol) and diethylmalonate (16 g; 100 mmol) were boiled in benzene (30 ml) in the presence of two drops of piperidine with azeotropic removal of water for 4 hr and diethyl benzalmalonate (10 g; 40 mmol) distilled, b.p. 122°C at 0.5 mmHg (lit.,[188] 195°C at 11 mmHg) as a colourless liquid.

3.6.6 Tosylazide

Tosyl azide (40%) was prepared by the method of Curtius[189]. A methanolic solution of tosyl chloride was treated with sodium azide dissolved in the minimum of water. The mixture was then diluted with water, the two layers separated, the non-aqueous layer collected, washed with water and dried over sodium sulphate to give tosyl azide, which was not further purified.

3.6.7 cis-N-Ethyl-3-thiocyanoacrylamide

This compound (45%), m.p. 135-137°C (lit.,[180] 144-145°C), was prepared by the method of Crow and Leonard from N-ethylpropiolamide and ammonium thiocyanate.

cis-N-Methyl-3-thiocyanoacrylamide (50%), m.p. 120-122°C (lit.,[180] 129-130°C dec.) was also prepared by this method, from N-methylpropiolamide and ammonium thiocyanate.

cis-Thiocyanoacrylamide was made in collaboration with C.J. McGregor from the reaction of propiolamide with ammonium thiocyanate.

3.6.8 Phenacyltriphenylphosphonium bromide

Triphenylphosphine (7.86 g; 30 mmol) and phenacyl bromide (6 g; 30 mmol) were stirred in boiling benzene (30 ml) for 3 hr. The cooled reaction mixture was filtered to afford the phosphonium salt (12.45 g; 27 mmol) as white crystals, m.p. 272-273°C (from ethanol/hexane) (lit.,[92] 269-271°C from water; 279-280°C from methanol/ethyl acetate).

3.6.9 Triphenylphosphonium phenacylide

This compound (99%), m.p. 179-180°C (lit.,[92] 178-179°C) was prepared by the procedure described by Ramirez and Dershowitz[92].

3.7 Reactions of arsonium ylides with N-ethyl-3-isothiazolone

3.7.1 Reaction with stabilised ylides

(i) cis-N-Ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide

To a stirred solution of carbomethoxymethyltriphenylarsonium bromide (1.24 g; 2.7 mmol) and N-ethyl-3-isothiazolone (0.32 g; 2.5 mmol) in anhydrous methanol (15 ml) under nitrogen at 0°C was added sodium metal (0.058 g; 2.5 mmol). The reaction mixture was allowed to rise to room temperature overnight and the solvent removed in vacuo to give an oil (1.6 g) which was chromatographed on 6% deactivated alumina (1" x 4.25"). Elution with ethyl acetate-ethanol (9:1) gave cis-N-ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide (0.35 g; 27.6%) as a white solid, m.p. 89-93°C.

Found: C, 61.32; H, 5.14; N, 2.49%

$C_{26}H_{26}AsNO_3S$ requires: C, 61.53; H, 5.16; N, 2.76%

N.m.r. δ_H 7.9-7.1 (15H, c, phenyl protons), 6.53 (1H, d, J = 10.6 Hz, olefinic proton), 6.4 (1H, br s, NH), 5.51 (1H, d, J = 10.6 Hz, olefinic proton), 3.57 (br s, part of CO_2CH_3 signal), 3.3-2.9 (2H, m, centred at 3.11 p.p.m., CH_2), 2.7 (br, s, part of CO_2CH_3 signal), 0.96 (3H, t, J = 7.2 Hz, CH_2-CH_3), total integration correct. On cooling, the two portions of the CO_2CH_3 signal move closer together and separate upon warming.

I.r. ν_{max} 3285 (NH), 1635 (C=O), 1570 (C=O) cm^{-1}.

A better analytical sample was obtained as colourless crystals when the ylide was stirred in a benzene solution of methyl iodide at room temperature for 5 days, and then precipitated with ether (see section 3.8.3), m.p. 133.5-135.5°C.

Found: C, 61.79; H, 5.13; N, 2.69%

$C_{26}H_{26}AsNO_3S$ requires: C, 61.53; H, 5.16; N, 2.76%

Alternatively, cis-N-ethyl-3-(carbomethoxymethylene-triphenylarsenanylmercapto)acrylamide could be prepared in the absence of solvent. Triphenylarsonium carbomethoxymethylide (0.56 g; 1.5 mmol) and N-ethyl-3-isothiazolone (0.2 g; 1.55 mmol) were stirred in a melt at 70°C under nitrogen for 2 hr. The reaction mixture was chromatographed on 6% deactivated alumina (1.25"x5") and the title compound eluted with ethanol-ethylacetate (1:9). The product precipitated out of a concentrated solution of eluent as a white powder (0.166 g; 22%), m.p. 126-127°C. The spectra of the powder were identical to those of an authentic sample.

The reaction did not proceed in benzene at room temperature.

(ii) cis-N-Ethyl-3-(phenacylidenetriphenylarsenanyl-mercapto)acrylamide

To phenacyltriphenylarsonium bromide (3.4 g; 6.8 mmol) suspended in anhydrous ethanol (15 ml) under nitrogen at 0°C was added sodium metal (0.086 g; 6.6 mmol) with stirring. The arsonium salt disappeared over 5 min and a further 5 min elapsed before the dropwise addition of N-ethyl-3-isothiazolone (0.85 g; 6.6 mmol) in anhydrous ethanol (15 ml). The reaction mixture was stirred overnight during which time a precipitate appeared which was collected by filtration

(0.14 g; unreacted arsonium salt). The filtrate was evaporated *in vacuo* to afford an oil (4.27 g) which was chromatographed on 6% deactivated alumina (3" x 3.5"). Elution with ethyl acetate gave *cis*-*N*-ethyl(phenacylidene-triphenylarsenanylmercapto)acrylamide (2.01 g; 53%) as colourless needles from dichloromethane, m.p. 159-161.5°C,

Found: C, 60.07; H, 4.49; N, 1.59%

$C_{31}H_{28}AsNO_2S.CH_2Cl_2$ requires: C, 60.19; H, 4.73; N, 2.19%

and from chloroform-*n*-hexane, m.p. 184-185°C.

Found: C, 57.39; H, 4.15; N, 1.78%

$C_{31}H_{28}AsNO_2S.CHCl_3$ requires: C, 57.11; H, 4.34; N, 2.08%

N.m.r. δ_H 7.9-7.2 (21H, *c*, aromatic protons, $C\underline{H}Cl_3$), 6.57 (1H, *d*, J = 10 Hz, olefinic proton), 5.9 (1H, *br s*, NH, sharpened by irrad^{n} of *A*) (*B*), 5.38 (1H, *d*, J = 10 Hz, olefinic), 3.3-3.0 (2H, *m*, collapsed by irrad^{n} of *B* to a quartet, J = 7.6 Hz, centred at 3.02 p.p.m., CH_2) (*A*), 0.88 (3H, *t*, J = 7.6 Hz, CH_3), total integration correct.

I.r. ν_{max} 3260 (NH), 1642 (C=O), 1580 (C=O) cm^{-1}.

3.7.2 Reaction with semi-stabilised ylides

(i) N-Ethyl-cis-3-(α-ethoxybenzyl)mercaptoacrylamide

Benzyltriphenylarsonium bromide (1.2 g; 2.5 mmol) and *N*-ethyl-3-isothiazolone (0.33 g; 2.7 mmol) were dissolved together in anhydrous ethanol (15 ml) at 0°C and sodium metal (0.058 g; 2.5 mmol) was added with stirring. The solution immediately developed an orange colouration which gradually faded to a faint yellow. After one hour at 0°C the reaction mixture was allowed to rise to room temperature during which time a colourless solid deposited which was collected by filtration and identified as triphenylarsine (0.070 g),

m.p. 56.5-57.5°C (lit.,[16] 60.5°C) by spectroscopic comparison with an authentic sample. The filtrate was evaporated *in vacuo* and the resultant oil (0.87 g) chromatographed on 6% deactivated alumina (1.25" x 6"). Petrol-ether (1:1) removed more triphenylarsine (0.42 g; 64% overall yield) and petrol-ether (1:4) eluted N-ethyl-*cis*-3-(α-ethoxybenzyl)mercaptoacrylamide as a colourless solid (0.35; 53%). Recrystallisation from benzene/hexane gave an analytical sample as colourless plates, m.p. 99-100°C.

Found: C, 63.14; H, 7.13; N, 5.25%. p^+:265

$C_{14}H_{19}NO_2S$ requires: C, 63.36; H, 7.22; N, 5.28%. p^+:265

N.m.r. δ_H 7.52-7.00 (5H, *c*, phenyl protons), 6.83 (1H, *d*, J = 9.8 Hz, olefinic proton), 6.26 (1H, *br t*, J = 5.5 Hz, NH) (*C*), 5.81 (1H, *d*, J = 9.8 Hz, olefinic proton), 5.6 (1H, *s*, CH), 4.05-3.3 (2H, *m*, collapsed by irrad^n of *B* $O-CH_2$). 3.21 (2H, *m*, collapsed by irrad^n of *C* $N-CH_2$) (*A*), 1.2 (3H, *t*, J = 7 Hz, $O-CH_2-CH_3$) (*B*), 1.01 (3H, *t*, J = 7 Hz, collapsed by irrad^n of *A* $N-CH_2-CH_3$), total integration correct.

I.r. ν_{max} 3309 (NH), 1648 (C=O) cm^{-1}.

(ii) N-Ethyl-cis-3-(α-methoxybenzyl)mercaptoacrylamide

To a stirred solution of benzyltriphenylarsonium bromide (1.2 g; 2.5 mmol) and *N*-ethyl-3-isothiazolone (0.33 g; 2.7 mmol) in anhydrous methanol (15 ml) at 0°C was added sodium metal (0.058 g; 2.5 mmol) and the resultant yellow solution was allowed to rise to room temperature. After 24 hr the reaction mixture was evaporated *in vacuo* and the resultant oil (1.8 g) chromatographed on 6% deactivated alumina (1.25" x 6"). Elution with hexane gave triphenylarsine (0.62 g; 80%)

as indicated by its i.r. spectrum. Further elution with ether gave N-ethyl-cis-3-(α-methoxybenzyl)mercaptoacrylamide (0.4 g; 63.7%) as colourless needles (from ether at -15°C), m.p. 74-75°C.

Found: C, 62.20; H, 6.87; N, 5.44%. p^+:251.

$C_{13}H_{17}NO_2S$ requires: C, 62.12; H, 6.82; N, 5.57%. p^+:251.

N.m.r. δ_H 7.5-7.2 (5H, c, phenyl protons), 6.85 (1H, d, J = 10.1 Hz, olefinic proton), 5.94 (1H, br s, NH), 5.80 (1H, d, J = 10.1 Hz olefinic proton), 5.56 (1H, s, CH), 3.48 (3H, s, OCH_3), 3.28 (2H, m, two coupling constants J = 7.25 Hz and J = 5.9 Hz, CH_2, collapsed to quartet, J = 7.25 Hz, by D_2O shake), 1.09 (3H, t, J = 7.25 Hz, CH_2-CH_3), total integration correct.

I.r. ν_{max} 3280 (NH), 1660 (C=O) cm^{-1}.

(iii) N-Ethyl-cis-3-[α-methoxy(p-bromobenzyl)]mercapto-acrylamide

p-Bromobenzyltriphenylarsonium bromide (1.39 g; 2.5 mmol) and N-ethyl-3-isothiazolone (0.33 g; 2.6 mmol) were dissolved together in anhydrous methanol (15 ml) at 0°C and sodium metal (0.058 g; 2.5 mmol) was added with stirring. An immediate pink colouration developed which became yellow overnight. The reaction mixture was evaporated in vacuo and the resultant oil (1.8 g) chromatographed on 6% deactivated alumina (1.25" x 6"). Elution with petrol gave triphenylarsine (0.59 g; 77.2%) as indicated by its i.r. spectrum. Further elution with dichloromethane gave N-ethyl-cis-3-[α-methoxy(p-bromobenzyl)]mercaptoacrylamide (0.6 g; 78%) as a syrup. The syrup was dissolved in the minimum ether and kept at -15°C for 7 days to give the title

compound as pale yellow crystals, m.p. 95-96°C.

Found: C, 47.53; H, 4.91; N, 4.03%. p^+:331.

$C_{13}H_{16}BrNO_2S$ requires: C, 47.28; H, 4.88; N, 4.24%. p^+:331.

N.m.r. δ_H 7.5-7.2 (4H, c, aromatic protons), 6.74 (1H, d, J = 9.8 Hz, olefinic proton), 6.20-5.95 (1H, br t, unaffected by D_2O shake, NH), 5.82 (1H, d, J = 9.8 Hz, olefinic proton), 5.49 (1H, s, CH) 3.46 (3H, s, OCH_3), 3.4-3.1 (2H, c, unaffected by D_2O shake, CH_2), 1.09 (3H, t, J = 7.2 Hz, CH_2-CH_3), total integration correct.

I.r. ν_{max} 3290 (NH), 3090, 1630 (C=O) cm^{-1}.

(iv) N-Ethyl-cis-3-[α-ethoxy(p-bromobenzyl)]mercapto-acrylamide

p-Bromobenzyltriphenylarsonium bromide (1.39 g; 2.5 mmol) and N-ethyl-3-isothiazolone (0.33 g; 2.6 mmol) were dissolved together in anhydrous ethanol (15 ml) at 0°C and sodium metal (0.058 g; 2.5 mmol) was added with stirring. An immediate pink colouration developed which became yellow overnight. The reaction mixture was evaporated in vacuo and the resultant oil (1.9 g) chromatographed on 6% deactivated alumina (1.25" x 5"). Elution with petrol gave triphenylarsine (0.7 g; 91.2%) as indicated by its i.r. spectrum. Further elution with dichloromethane gave N-ethyl-cis-3-[α-ethoxy)p-bromobenzyl)] mercaptoacrylamide (0.7 g; 81.2%) as a syrup which would not solidify, even after prolonged trituration.

The mass spectrum showed the correct parent ion p^+:343.

Found: 343.024056 and 345.019078.

$C_{14}H_{18}BrNO_2S$ requires: 343.024209 (^{79}Br) and 345.022239 (^{81}Br).

N.m.r. δ_H 7.7-7.1 (4H, c, aromatic protons), 6.77 (1H, d, J = 10 Hz, olefinic proton), 6.36-6.1 (1H, br t, J = 5 Hz,

irrad^{n} at B collapses to broad singlet, NH) (A), 5.85 (1H, d, J = 10 Hz, olefinic proton), 5.59 (1H, s, CH) 4.0-3.1 (4H, c, irrad^{n} at C collapses low field multiplet to AB quartet, J = 9 Hz, δ_{AB} = 0.348 p.p.m. centred at δ3.695, OCH_2 (B); irrad^{n} at D collapses high field multiplet to a doublet, J = 5 Hz, centred at δ3.25, NCH_2), 1.24 (3H, t, J = 7.6 Hz, $OCH_2\underline{CH_3}$) (C), 1.08 (3H, t, J = 7 Hz, $NCH_2\underline{CH_3}$), total integration correct.

I.r. ν_{max} 3305 (NH), 1635 (C=O) cm^{-1}.

(v) N-Ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide

To a stirred solution of p-nitrobenzyltriphenylarsonium bromide (1.74 g; 3.34 mmol) in anhydrous ethanol (15 ml) at -10°C was added sodium metal (0.075 g; 3.1 mmol), whereupon the violet colour of the ylide appeared immediately. The solution was stirred for 5 min under nitrogen and N-ethyl-3-isothiazolone (0.4 g; 3.1 mmol) in anhydrous ethanol (20 ml) added dropwise over a further 5 min during which time the solution developed an intense red colouration which gradually faded overnight. A precipitate (0.23 g; NaBr) was filtered off and the filtrate evaporated in vacuo to give a yellow oil (2 g) which was chromatographed on 6% deactivated alumina (1.25" x 5.7"). Elution with ether gave triphenylarsine (0.15 g; 0.5 mmol) indentified by its n.m.r. Elution with ethylacetate gave N-ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide (0.54 g; 64%) as yellow crystals, m.p. 134-135°C (from chloroform/hexane).

Found: C, 53.88; H, 5.16; N, 10.31%. p^{+}:266.

$C_{12}H_{14}N_2O_3S$ requires: C, 54.12; H, 5.29; N, 10.51%. p^{+}:266.

N.m.r. δ_H 8.17 (2H, d, J = 9 Hz, aromatic protons ortho to nitro group), 7.5 (2H, d, J = 9 Hz, aromatic protons meta to nitro group), 6.7 (1H, d, J = 9.5 Hz, olefinic proton), 5.75 (1H, d, J = 9.5 Hz, olefinic proton), 5.6 (1H, br s, NH), 3.94 (2H, s, CH_2-S), 3.31 (2H, dd, two coupling constants J = 7.2 Hz and J = 5.4 Hz, CH_2-CH_3), 1.12 (3H, t, J = 7.2 Hz, CH_3), total integration correct.

I.r. ν_{max} 3350 (NH), 1635 (C=O) cm^{-1}.

Elution with ethyl acetate-methanol (5:1) gave triphenylarsine oxide (0.74 g; 2.3 mmol), m.p. 163-184°C, (lit.,[190] 170°C) identified by spectroscopic comparison with an authentic sample.

Repeating the reaction using p-nitrobenzyltriphenylarsonium bromide (1.68 g; 3.2 mmol), sodium metal (0.075 g; 3.1 mmol) and N-ethyl-3-isothiazolone (0.4 g; 3.1 mmol) in ethanol (35 ml) and heating the reaction mixture under reflux for 48 hr after addition of N-ethyl-3-isothiazolone gave triphenylarsine (0.32 g; 1.04 mmol), N-ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide (0.62 g; 2.33 mmol; 75%), and triphenylarsine oxide (0.70 g; 2.17 mmol), upon chromatographic work-up of the reaction mixture.

When the reaction was carried out using tris(p-chlorophenyl)-p-nitrobenzylarsonium tetrafluoroborate (0.95 g; 1.5 mmol), sodium metal (0.032 g; 1.4 mmol) and N-ethyl-3-isothiazolone (0.18 g; 1.4 mmol) in anhydrous ethanol (30 ml) at -20°C before allowing warming to room temperature, a poor yield of N-ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide (0.05 g; 0.19 mmol; 13.6%) was obtained.

(vi) Reaction with triphenylarsonium benzylide in THF

The orange ylide was generated in anhydrous THF

(30 ml) under nitrogen by adding 1.6 M butyllithium (1.93 ml; 3.1 mmol) to a stirred suspension of benzyltriphenylarsonium bromide (1.63 g; 3.4 mmol) at -20°C. After 5 min. N-ethyl-3-isothiazolone (0.4 g; 3.1 mmol) in anhydrous THF (20 ml) was added dropwise. The now brown suspension was allowed to rise to room temperature overnight, and then filtered to recover benzyltriphenylarsonium bromide (0.44 g; 27%), m.p. 141-143°C, identified by its n.m.r. The filtrate was evaporated *in vacuo* to give a gum (1.71 g) which was chromatographed on 6% deactivated alumina (1.25" x 8.75"). Only two products were eluted from the column. Elution with hexane-ether (3:2) gave triphenylarsine (0.564 g; 1.84 mmol), identified by its n.m.r. Elution with ethyl acetate gave a yellow powder (0.117 g), recrystallised from chloroform/hexane as yellow crystals, m.p. 106-108°C. I.r. ν_{max} 3280, 1630 (br), 1575, 1250, 1175 cm^{-1}. The mass spectrum showed the parent ion, p^+:159.

Found: 159.092728.

(vii) Reaction with triphenylarsonium p-nitrobenzylide in THF

The pink ylide was generated in anhydrous THF (20 ml) under nitrogen by adding sodium hydride (0.074 g; 3.1 mmol) to a stirred suspension of p-nitrobenzyltriphenylarsonium bromide (1.85 g; 3.5 mmol) at -10°C. After 5 min N-ethyl-3-isothiazolone (0.4 g; 3.1 mmol) in anhydrous THF (10 ml) was added dropwise. The red reaction mixture was stirred overnight at room temperature and evaporated *in vacuo* to give an oil (2.5 g) which was chromatographed on 6% deactivated alumina (1.25" x 12"). Elution with

petrol-ether (1:1) gave triphenylarsine (0.703 g; 2.29 mmol), identified by its n.m.r. Elution with ether-ethylacetate (1:1) gave trans-(4,4'-dinitro)stilbene (0.199 g; 0.73 mmol; p^+:270), recrystallised from chloroform/hexane as yellow crystals, m.p. 303-304.5°C (lit.,[191] 289.5-291°C). Further elution with ether-ethylacetate (1:1) gave an oil (0.290 g), containing N-ethyl-3-isothiazolone as shown by t.l.c. and n.m.r. No other products could be eluted from the solumn.

(viii) cis-N-Ethyl-3-(p-nitrobenzylidenetriphenyl arsenanylmercapto)acrylamide

To p-nitrobenzyltriphenylarsonium bromide (1.73 g; 3.34 mmol) dissolved in anhydrous ethanol (10 ml) under nitrogen at -10°C was added sodium metal (0.071 g; 3.1 mmol) with stirring, whereupon the red colouration of the ylide appeared immediately. After 5 min, N-ethyl-3-isothiazolone (0.4 g; 3.1 mmol) was added and the intense red colour of the title compound developed. A further 5 min elapsed and then the solvent was removed in vacuo, anhydrous benzene (15 ml) added, and the solution filtered to afford a purple oil (1.72 g) upon evaporation of the benzene. A n.m.r. (60 MHz) spectrum of the oil was similar to that of N-ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide with a triphenylarsine impurity. The title compound could not be isolated.

3.7.3 Reaction with triphenylarsonium isopropylide

The yellow ylide was generated in anhydrous THF (20 ml) under nitrogen by adding 1.6 M butyllithium (1.7 ml; 2.2 mmol) to a stirred suspension of

isopropyltriphenylarsonium tetrafluoroborate (1 g; 2.29 mmol) at -50°C. After 5 min, N-ethyl-3-isothiazolone (0.28 g; 2.2 mmol) in anhydrous THF (20 ml) was added dropwise. At first the colour faded to a pale yellow but was brown after 5 hr stirring at room temperature. T.l.c. indicated that all of the N-ethyl-3-isothiazolone had been used up. The reaction mixture was evaporated *in vacuo* to give a brown oil (1.5 g). Trituration of the oil with dichloromethane gave a brown solid (0.6 g) which, on boiling in ethanol, gave 2,4-bis-(N-ethylcarboxamide)methylene-1,3-dithietane as a white solid (0.070 g; 24.6%), m.p. 280°C (lit.,[130] 268-270°C).

I.r. ν_{max} 3320 (NH), 1620 (C=O) cm^{-1}.

The mass spectrum showed the required parent ion, p^+:258.

The dichloromethane leachings were evaporated *in vacuo* to give a yellow oil (0.9 g) which was chromatographed on 6% deactivated alumina (1" x 6"). Petrol eluted triphenylarsine (0.43 g; 1.4 mmol), identified by its i.r. Further elution with ether gave N-ethyl-*cis*-3-phenylmercaptoacrylamide (0.1 g; 21.9%), m.p. 115.5-118°C (lit.,[130] 128-129°C).

I.r. ν_{max} 3265 (NH), 1630 (C=O) cm^{-1}.

The mass spectrum showed the required parent ion, p^+:207.

Elution with ethyl acetate gave triphenylarsine oxide (0.030 g; 0.1 mmol), identified by its i.r.

3.8 Miscellaneous reactions of acrylamides

3.8.1 Reaction of cis-N-ethyl-3-thiocyanoacrylamide with arsonium ylides

(i) Reaction with triphenylarsonium benzylide

To benzyltriphenylarsonium bromide (1.22 g;

2.5 mmol) and cis-N-ethyl-3-thiocyanoacrylamide (0.43 g; 2.7 mmol) stirred in anhydrous ethanol (10 ml) at 0°C was added sodium metal (0.058 g; 2.5 mmol). The yellow solution was left stirring overnight, the solvent removed in vacuo and trituration with ether afforded benzyltriphenylarsonium bromide (0.24 g; 19.6%) and an orange oil (0.8 g) chromatographed on 6% deactivated alumina (1.25" x 6") to give, on elution with mixtures of petrol and ether, triphenylarsine (0.52 g; 1.7 mmol), N-ethyl-cis-3-(α-ethoxybenzyl)mercaptoacrylamide (0.076 g; 0.3 mmol) and N-ethyl-cis-benzylmercaptoacrylamide (0.14 g; 0.6 mmol), all identified by spectroscopic comparison with authentic samples.

(ii) Reaction with triphenylarsonium p-nitrobenzylide

To a stirred solution of p-nitrobenzyl-triphenylarsonium bromide (1.31 g; 2.5 mmol) and cis-N-ethyl-3-thiocyanoacrylamide (0.44 g; 2.8 mmol) in anhydrous ethanol (13 ml) at 0°C was added sodium metal (0.058 g; 2.5 mmol). The orange reaction mixture was left stirring overnight and then quenched with water (10 ml) and extracted with dichloromethane (2x10 ml). The organic extracts were evaporated in vacuo to afford an oil (1.14 g) which was chromatographed on 6% deactivated alumina (1.25" x 7"). Elution with hexane-ether (4:1) gave triphenylarsine (0.47 g; 1.26 mmol), identified by its i.e. Elution with hexane-ether (1:1) gave 2-imino-3-ethyl-4-oxo-2,3-dihydro-1,3-4H-thiazine (0.022 g; 0.14 mmol), sublimed (70°C/0.5 mmHg) as colourless crystals, m.p. 102.5-103°C.

Found: C, 46.21; N, 5.17; H, 17.99%. p^+:156.

$C_6H_8N_2OS$ requires: C, 46.10; H, 5.17; N, 17.92%. p^+:156.

N.m.r. δ_H 8.0-7.5 (1H, br, NH), 6.99 (1H, d, J = 10.4 Hz, olefinic proton α to sulphur), 6.28 (1H, d, J = 10.4 Hz, olefinic proton β to sulphur), 4.20 (2H, q, J = 7.0 Hz, N-CH_2), 1.23 (3H, t, J = 7.0 Hz, CH_3), total integration correct.

I.r. ν_{max} 3285 (NH), 1655 (C=O) cm^{-1}.

Further elution with hexane-ether (2:3) gave N-ethyl-cis-3-ethylmercaptoacrylamide (0.101 g; 0.64 mmol), m.p. 95-96°C (lit.,[130] 113-115°C).

The mass spectrum showed the required parent ion, p^+:159

Found: 159.072479

$C_7H_{13}NOS$ requires: 159.071781

Elution with n-propanol gave N-ethyl-cis-3-(p-nitrobenzyl)mercaptoacrylamide (0.18 g; 0.68 mmol), identified by spectroscopic comparison with an authentic sample.

3.8.2 Attempted synthesis of 2-imino-3-ethyl-4-oxo-2,3-dihydro-1,3-4H-thiazine

(i) cis-N-Ethyl-3-thiocyanoacrylamide (1.0 g; 6.4 mmol) was sublimed (100°C; 1.0 mmHg) to give colourless prisms (0.79 g; 79%), m.p. 118-119°C (lit.,[180] 144-145°C) whose spectra were identical to those of authentic cis-N-ethyl-3-thiocyanoacrylamide.

Found: C, 45.86; H, 5.16; N, 17.62%. p^+:156.

$C_6H_8N_2OS$ requires: C, 46.10; H, 5.17; N, 17.92%. p^+:156.

I.r. ν_{max} 3320 (NH), 2170 (C≡N), 1635 (C=O) cm^{-1}.

(ii) cis-N-Ethyl-3-thiocyanoacrylamide (1.2 g; 7.7 mmol) was heated in a bunsen flame for a short time and then sublimed (50°C; 0.3 mmHg) to give N-ethyl-3-isothiazolone

(0.8 g; 81%), m.p. 57-58°C (lit.,[180] 61-62°C). The spectra of the sublimed product were identical to those of authentic N-ethyl-3-isothiazolone.

Found: C, 46.26; H, 5.40; N, 10.66%.

C_5H_7NOS requires: C, 46.48; H, 5.46; N, 10.84%.

I.r. ν_{max} 1600 (br) (C=O) cm^{-1}.

3.8.3 Attempted methylation of cis-N-ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide

(i) To cis-N-ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide (0.3 g; 0.6 mmol) dissolved in anhydrous benzene (15 ml) was added methyl iodide (0.04 ml; 0.6 mmol) dropwise with stirring. The reaction mixture was stirred under nitrogen at room temperature for 5 days. Upon the addition of ether (5 ml), a white solid precipitated which was identified as the starting ylide (0.2 g; 67%), m.p. 133.5-135.5°C.

Found: C, 61.79; H, 5.13; N, 2.69%.

$C_{26}H_{26}AsNO_3S$ requires: C, 61.53; H, 5.16; N, 2.76%

I.r. ν_{max} 3285 (NH), 1635 (C=O), 1570 (C=O) cm^{-1}.

(ii) cis-N-Ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide (0.18 g; 0.35 mmol), methyl iodide (0.02 ml; 0.35 mmol) and anhydrous benzene (5 ml) were heated at 92°C in a sealed tube for 20 hr. Evaporation of solvents in vacuo gave a red-brown oil (0.2 g) which was chromatographed on 6% deactivated alumina (1" x 2.25"). Elution with petrol-ether (1:1) gave triphenylarsine (0.030 g; 0.1 mmol), identified by its i.r. Elution with ether gave N-ethyl-3-isothiazolone (0.010 g; 0.08 mmol),

identified by its i.r. Elution with ether-ethyl acetate (1:17) gave triphenylarsine oxide (0.080 g; 0.24 mmol), ν_{max} 880 (As=O) cm^{-1}, identified by its i.r. No other products could be isolated from the column.

3.8.4 Thermolysis of arsenanylmercaptoacrylamides

(i) Kugelrohr thermolysis of cis-N-ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide

cis-N-Ethyl-3-(carbomethoxymethylenephenylarsenanylmercapto)acrylamide (0.19 g; 0.37 mmol) was heated in a Kugelrohr at 100°C at 0.2 mmHg for 30 hr. The sublimate (0.040 g) was shown by n.m.r. to contain only triphenylarsine (8.5 mg; 7.5%) and N-ethyl-3-isothiazolone (31.5 mg, 65.9%). N.m.r. showed that the residue (0.16 g) contained triphenylarsine, starting ylide, N-ethyl-3-isothiazolone, and a new compound with two doublets, J = 12 Hz. Only triphenylarsine (44.2 mg; 46.5% overall and N-ethyl-3-isothiazolone (13.5 mg; 94.3% overall) could be isolated from am alumina preparative t.l.c. plate using ethyl acetate : ether (2:1) as the eluent.

(ii) Thermolysis of cis-N-ethyl-3-(phenacylidene-triphenylarsenanylmercapto)acrylamide in toluene

cis-N-Ethyl-3-(phenacylidenetriphenylarsenanylmercapto)acrylamide $CHCl_3$ (0.6 g; 0.89 mmol) was heated under reflux in anhydrous toluene (10 ml) for 14 hr. The toluene was removed in vacuo and the remaining oil triturated with ether to give a residue (0.23 g) and a filtrate (0.21 g). The residue was chromatographed on 6% deactivated alumina.

Elution with ether-petrol (1:1) gave a white solid, trans-1,2,3-tribenzoylcyclopropane (0.070 g; 0.2 mmol), m.p. 216-217.5°C (from $CDCl_3$) (lit.,[192] 219-220°C).

Found: C, 80.12; H, 5.07%.

$C_{24}H_{18}O_3$ requires: C, 81.33; H, 5.08%.

The mass spectrum showed the required parent ion, p^+:354.

Found: 354.125673.

$C_{24}H_{18}O_3$ requires: 354.125586.

Elution with ethanol-ethylacetate (1:1) gave an oil (0.16 g), triturated with ether to give insoluble triphenylarsine oxide (0.050 g), ν_{max} 880 cm^{-1}. and an oil (0.080 g) containing triphenylarsine oxide and N-ethyl-3-isothiazolone as indicated by n.m.r. and i.r. Elution with ethanol afforded triphenylarsine oxide (0.1 g; 0.31 mmol), identified by its i.r.

The ether leachings were chromatographed on 6% deactivated alumina. Elution with petrol gave triphenylarsine (0.12 g; 0.39 mmol), identified by its n.m.r. Elution with ethanol gave triphenylarsine oxide (0.09 g; 0.28 mmol), identified by its i.r.

(iii) Thermolysis of cis-N-ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide in benzene

cis-N-Ethyl-3-(carbomethoxymethylenetriphenylarsenanylmercapto)acrylamide (0.56 g; 1.1 mmol) was heated under reflux in anhydrous benzene (15 ml) for 28 hr. T.l.c. on alumina showed mainly unreacted ylide and no products were isolated by chromatography.

3.8.5 Attempted oxidation of cis-N-ethyl-3-(carbomethoxy-methylenetriphenylarsenanylmercapto)acrylamide

To a cooled solution of cis-N-ethyl-3-(carbomethoxy-methylenetriphenylarsenanylmercapto)acrylamide (1.52 g; 2.99 mmol) in dry dichloromethane (10 ml), 85% m-chloroperbenzoic acid (0.01 g) in dichloromethane (10 ml) was added dropwise under nitrogen. There was no instantaneous precipitate of m-chlorobenzoic acid. The reaction mixture was left stirring at room temperature overnight, evaporated in vacuo and then put down a 6% deactivated alumina column (1.25" x 13.5"). Petrol eluted triphenylarsine (0.43 g; 1.4 mmol), identified by its i.r. Ethylacetate eluted N-ethyl-3-isothiazolone (0.21 g; 1.6 mmol), identified by spectroscopic comparison with an authentic sample. Elution with ethanol gave triphenyl-arsine oxide (0.010 g; 0.03 mmol), identified by its i.r.

3.8.6 Attempted reduction of cis-N-ethyl-3-(carbomethoxy-methylenetriphenylarsenanylmercapto)acrylamide

cis-N-Ethyl-3-(carbomethoxymethylenetriphenylarsenanyl-mercapto)acrylamide (1.51 g; 2.97 mmol) in chloroform (10 ml) and acetic acid (30 ml) was warmed with zinc dust (7.4 g) until this had dissolved. The resultant solution was washed repeatedly with water, dried over anhydrous sodium sulphate and evaporated in vacuo to give an oil (0.66 g) which was chromatographed on 6% deactivated alumina (1" x 4.5"). Elution with petrol gave triphenylarsine (0.47 g; 1.54 mmol), identified by its i.r. spectrum, as the only product obtained from the column. Neutralisation of the aqueous mother liquors with sodium bicarbonate, followed by extration with

dichloromethane, drying over anhydrous sodium sulphate, and evaporation *in vacuo* gave an oil (0.28 g) which was chromatographed on 6% deactivated alumina (1" x 3.75"). Elution with petrol gave triphenylarsine (0.030 g; 0.1 mmol), which was the only product eluted from the column.

3.8.7 *Attempted cyclisations of N-ethyl-cis-(α-alkoxybenzyl)-mercaptoacrylamides*

(i) *N*-Ethyl-*cis*-(α-methoxybenzyl)mercaptoacrylamide (0.282 g; 1.1 mmol) was heated in a Kugelrohr at 150°C at 2 mmHg for 4 hr. The remaining orange oil (0.223 g) was chromatographed on 6% deactivated alumina (1.25" x 4") to give a band eluted with ethylacetate. Evaporation *in vacuo* afforded a white gum (0.117 g). Proton n.m.r. and i.r. seemed to indicate a mixture and the absence of any methoxy groups.

Mass spectra:- 438.145984; $C_{24}H_{26}N_2O_2S_2$ requires 438.143562.
308.109699; $C_{19}H_{18}NOS$ requires 308.110905.
$C_{16}H_{22}NOS_2$ requires 308.114275.

I.r. ν_{max} 3330 (NH), 1630 (br) (C=O) cm^{-1}.

Thermolysis was unsuccessful at 110°C at 0.001 mmHg, with 82% recovery of the acrylamide. However, at 140°C at 0.001 mmHg the acrylamide sublimed without rearrangement.

(ii) The cyclisation of N-ethyl-*cis*-(α-ethoxybenzyl)-mercaptoacrylamide using potassium *tert*-butoxide as the base was attempted in an n.m.r. tube. To *N*-ethyl-*cis*-(α-ethoxybenzyl)mercaptoacrylamide (0.020 g; 0.07 mmol) dissolved in anhydrous THF was added a catalytic amount of $KOBu^t$. After 2 hr heating at 60°C, the n.m.r. spectrum was

unchanged. Thus, $KOBu^t$ did not bring about ring closure.

3.8.8 Attempted cyclisation of cis-N-methyl-3-thiocyanoacrylamide

cis-N-Methyl-3-thiocyanoacrylamide (0.2 g; 1.4 mmol) was sublimed (100°C; 0.5 mmHg) to give colourless crystals (0.16 g; 80%), m.p. 100-101.5°C (lit.,[180] 129-130°C). The spectra of the sublimed product were identical to those of authentic cis-N-methyl-3-thiocyanoacrylamide.

Found: C, 42.23; H, 4.25; N, 19.70%. p^+:142.
$C_5H_6N_2OS$ requires: C, 42.24; H, 4.30; N, 19.33%. p^+:142.
I.r. ν_{max} 3330 (NH), 3100, 2170 (C≡N), 1650 (C=O) cm^{-1}.

3.9 Decomposition of diazo-compounds in the presence of 3-isothiazolones

3.9.1 2,2-Bis(carbomethoxy)-3-ethyl-4-oxo-1,3-4H-thiazine

To a stirred solution of N-ethyl-3-isothiazolone (1.23 g; 9.5 mmol) in anhydrous benzene (10 ml) under nitrogen was added a suspension of rhodium (II) acetate (15 mg) in anhydrous benzene (5 ml). Dimethyldiazomalonate (1.42 g; 9 mmol) in anhydrous benzene (10 ml) was added dropwise over 5 min and the reaction mixture heated under reflux for 4 hr. The solvent was then evaporated in vacuo and the oil (2.7 g) crystallised from ether to give the title compound (1.65 g; 6.37 mmol; 70.1%). An analytical sample was obtained by recrystallisation from ether as colourless crystals, m.p. 133.5-135.0°C.

Found: C, 46.16; H, 5.18; N, 5.45%. p^+:259.
$C_{10}H_{13}NO_5S$ requires: C, 46.32; H, 5.05; N, 5.40%. p^+:259.

N.m.r. δ_H 7.75 (1H, d, J = 6 Hz, olefinic proton), 6.89 (1H, d, J = 6 Hz, olefinic proton), 3.62 (6H, s, CO_2CH_3), 4.2-3.2 (2H, m, irrad^n of A collapses the multiplet to an AB quartet, J = 10.5 Hz, δ_{AB} = 0.62 p.p.m. centred at δ 3.70, N-CH_2), 1.18 (3H, t, J = 7.8 Hz, CH_2-CH_3) (A), total integration correct.

I.r. ν_{max} 3060, 1740, 1660 cm^{-1}.

3.9.2 2-Acetyl-2-carbethoxy-3-ethyl-4-oxo-1,3-4H-thiazine

To a stirred solution of N-ethyl-3-isothiazolone (0.3 g; 2.3 mmol) in anhydrous benzene (5 ml) under nitrogen was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml). Diazo ethylacetoacetate (0.4 g; 2.5 mmol) in anhydrous benzene (5 ml) was added dropwise over 5 min and the reaction mixture heated under reflux for 1.5 hr. The solvent was removed in vacuo and the oil (0.6 g) crystallised from ether to give the title compound (0.44 g; 1.7 mmol; 74%). Recrystallisation from dichloromethane/ether gave the title compound as pale yellow needles, m.p. 120.5-121.5°C.

Found: C,51.22; H, 5.80; N, 5.42%. p^+:257.

$C_{11}H_{15}NO_4S$ requires: C,51.35; H, 5.85; N, 5.44%. p^+:257

N.m.r. δ_H 7.45 (1H, d, J = 6 Hz, olefinic proton), 6.87 (1H, d, J = 6 Hz, olefinic proton), 4.16 (2H, q, J = 7 Hz, $CO_2CH_2CH_3$), 4.0-3.2 (2H, m, AB type, N-CH_2), 2.44 (3H, s, CO.CH_3), 1.28 and 1.23 (6H, 2 x overlapping t, J = 6 Hz and 7 Hz respectively, NCH_2CH_3 and O-CH_2CH_3), total integration correct.

I.r. ν_{max} 3115, 3090, 3068, 1710, 1700, 1675 cm^{-1}.

3.9.3 2,2-Diacetyl-3-ethyl-4-oxo-1,3-4H-thiazine

To a stirred solution of N-ethyl-3-isothiazolone (0.3 g; 2.3 mmol) in anhydrous benzene (5 ml) under nitrogen was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml). Diazo acetylacetone (0.32 g; 2.5 mmol) in anhydrous benzene (5 ml) was added dropwise over 5 min and the reaction mixture heated under reflux for 1.5 hr. The solvent was removed *in vacuo* and the oil (0.6 g) crystallised from ether to give the title compound (0.3 g; 1.3 mmol; 58%). Recrystallisation from ether gave the title compound as colourless plates, m.p. 127.5-128°C.

Found: C, 52.69; H, 5.85; N, 6.06%. p^+:227.

$C_{10}H_{13}NO_3S$ requires: C, 52.85; H, 5.76; N, 6.16%. p^+:227.

N.m.r. δ_H 7.50 (1H, d, J = 6 Hz, olefinic proton), 6.92 (1H, d, J = 6 Hz, olefinic proton), 3.9-3.3 (2H, m, irrad^n of A collapses the multiplet to an AB quartet, J = 13.5 Hz, δ_{AB} = 0.37 p.p.m. centred at δ 3.59, N-CH_2), 2.4 (6H, s, Co.CH_3), 1.27 (3H, t, J = 7.4 Hz, CH_2CH_3) (A), total integration correct.

I.r. ν_{max} 1710, 1630, 1615 cm^{-1}.

3.9.4 Spiro[phenanthrene-9,2^1-(3-ethyl-4-oxo-1,3-4H-thiazine)]-10-one

To a stirred solution of N-ethyl-3-isothiazolone (0.3 g; 2.3 mmol) in anhydrous benzene (5 ml) under nitrogen was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml). 9-Diazo-10-phenanthrenone (0.55 g; 2.5 mmol) in anhydrous benzene (5 ml) was added dropwise over 5 min. The reaction mixture was then heated under reflux for 20 hr.

The solvent was removed *in vacuo* to afford an oil (0.9 g) which was triturated with ether and filtered to remove insoluble impurities. The filtrate was evaporated *in vacuo* to afford a brown solid (0.69 g; 2.1 mmol; 91.3%) which was shown by n.m.r. spectroscopy to be the title compound. Recrystallisation from ethanol gave the title compound as pale brown plates, m.p. 148-149.5°C.

Found: C, 70.83; H, 4.71; N, 4.19%. p^+:321.

$C_{19}H_{15}NO_2S$ requires: C, 71.00; H, 4.70; N, 4.36%. p^+:321.

N.m.r. δ_H 8.74-8.52 (2H, c, aromatic protons), 8.48-8.20 (2H, c, aromatic protons), 7.80-7.51 (4H, c, aromatic protons), 6.28 (1H, d, J = 5.8 Hz, olefinic proton), 6.07 (1H, d, J = 5.8 Hz, olefinic proton), 3.70 (2H, q, J = 7 Hz, $N-C\underline{H}_2-CH_3$), 1.10 (3H, t, J = 7 Hz, $N-CH_2-C\underline{H}_3$), total integration correct.

I.r. ν_{max} 1670 (br) (C=O) cm^{-1}.

3.9.5 Spiro[(2,2-dimethyl-4,6-dioxo-1,3-dioxan)-5,2^1-(3-ethyl-4-oxo-1,3-4H-thiazine)]

To a stirred solution of N-ethyl-3-isothiazolone (0.3 g; 2.3 mmol) in anhydrous benzene (5 ml) under nitrogen was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml). Meldrum's diazo (0.42 g; 2.5 mmol) in anhydrous benzene (10 ml) was added dropwise over 5 min. The reaction mixture was then heated under reflux for 9 hr. The solvent was removed *in vacuo* to afford an oil (0.7 g) which was triturated with ether to give the insoluble title compound as a brown solid (0.46 g; 1.7 mmol; 74%). Recrystallisation from chloroform/ether gave the title

compound as pale brown crystals, m.p. 162.5-163°C.

Found: C, 48.62; H, 4.71; N, 5.07%. p^+:271.

$C_{11}H_{13}NO_5S$ requires: C, 48.70; H, 4.83; N, 5.16%. p^+:271.

N.m.r. δ_H 7.62 (1H, d, J = 6 Hz, olefinic proton), 7.05 (1H, d, J = 6 Hz, olefinic proton), 4.18-3.25 (2H, m, irrad^n at A collapses multiplet to AB quartet, J = 16.8 Hz, δ_{AB} = 0.45 p.p.m. centred at δ3.69, NCH_2), 1.7 (6H, s, $C(CH_3)_2$), 1.35 (3H, t, J = 7.5 Hz, $N-CH_2-CH_3$) (A), total integration correct.

I.r. ν_{max} 1700 (sh), 1675 (br) (C=O) cm^{-1}.

3.9.6 Spiro[(5,5-dimethyl-1,3-dioxocyclohexane)-2,2^1-(3-ethyl-4-oxo-1,3-4H-thiazine)]

To a stirred solution of N-ethyl-3-isothiazolone (0.3 g; 2.3 mmol) and 2-diazo-5,5-dimethylcyclohexan-1,3-dione (0.42 g; 2.5 mmol) in anhydrous benzene (15 ml) was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml) dropwise over 5 min. The reaction mixture was then heated under reflux for 7 hr. The solvent was removed in vacuo to afford a brown oil (0.7 g) which was recrystallised from ether to give the title compound (0.4 g; 1.5 mmol; 65%) as pale brown crystals, m.p. 116-117°C. The mass spectrum showed the correct parent ion p^+:267.

Found: 267.093172.

$C_{13}H_{17}NO_3S$ requires: 267.092908

N.m.r. δ_H 7.54 (1H, d, J = 6.6 Hz, olefinic proton), 6.93 (1H, d, J = 6.6 Hz, olefinic proton), 4.0-3.2 (2H, m, irrad^n of A collapses the multiplet to an AB quartet,

J = 14 Hz, δ_{AB} = 0.47 p.p.m. centred at δ 3.73, N-C$\underline{H}_2$), 2.37 (4H, s, C$\underline{H}_2$CO), 1.32 (3H, t, J = 7.6 Hz, $CH_2C\underline{H}_3$)(A), 1.06 (6H, s, C(C$\underline{H}_3$)$_2$), total integration correct.
I.r. ν_{max} 1660, 1640 (C=O) cm^{-1}.

3.9.7 Decomposition of 2-diazoacenaphthen-1-one in the presence of N-ethyl-3-isothiazolone

To a stirred solution of N-ethyl-3-isothiazolone (0.3 g; 2.3 mmol) and 2-diazoacenaphthen-1-one (0.485 g; 2.5 mmol) in anhydrous benzene (15 ml) was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml) dropwise over 5 min. The reaction mixture was then heated under reflux for 6 hr. A brown precipitate (0.4 g; 1.2 mmol) was filtered off and recrystallised from dichloromethane to give orange needles of trans-[$\Delta^{1,1^1}$-bisacenaphthene]-2,2^1-dione, m.p. 299-300°C (lit.,[159] 291-292°C).

Found: C, 82.48; H, 3.52%.

$C_{24}H_{12}O_2$ requires: C, 86.73; H, 3.64%.

The mass spectrum showed the correct parent ion p^+:322.

Found: 322.082407.

$C_{24}H_{12}O_2$ requires: 322.083724.

I.r. ν_{max} 1700 (C=O), 1600 (C=C) cm^{-1}.

Evaporation of the filtrate, followed by sublimation (50°C; 0.5 mmHg) afforded N-ethyl-3-isothiazolone (0.25 g; 1.9 mmol), identified by spectroscopic comparison with an authentic sample.

3.9.8 Decomposition of ethyl diazoacetate in the presence of N-ethyl-3-isothiazolone

To a stirred solution of N-ethyl-3-isothiazolone (0.4 g;

3.2 mmol) and ethyl diazoacetate (0.42 g; 3.5 mmol) in anhydrous benzene (15 ml) was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml) dropwise over 5 min. The reaction mixture was then heated under reflux for 60 hr. T.l.c. indicated that the isothiazolone remained but the ethyldiazoacetate had decomposed. The reaction mixture was evaporated in vacuo, followed by sublimation (50°C; 0.5 mmHg) to afford N-ethyl-3-isothiazolone (0.4 g; 3.1 mmol), identified by spectroscopic comparison with an authentic sample.

3.9.9 Attempted decomposition of 1-diazo-2,3,4-triphenylcyclopentadiene in the presence of N-ethyl-3-isothiazolone

To a stirred solution of N-ethyl-3-isothiazolone (0.36 g; 2.8 mmol) and 1-diazo-2,3,4-triphenylcyclopentadiene (0.96 g; 3.0 mmol) in anhydrous benzene (15 ml) was added a suspension of rhodium (II) acetate (10 mg) in anhydrous benzene (5 ml). The reaction mixture was heated under reflux for 20 hr. T.l.c. and n.m.r. indicated that both the diazo compound and the isothiazolone were still present.

A similar reaction with 4,4^1-di-tert-butylphenylbenzoyldiazomethane also failed.

3.9.10 Spiro[(2,2-dimethyl-4,6-dioxo-1,3-dioxan)-5,2^1-(3-carbomethoxy-4-oxo-1,3-4H-thiazine)]

To a stirred solution of N-carbomethoxy-3-isothiazolone (0.37 g; 2.3 mmol) and Meldrum's diazo (0.43 g; 2.5 mmol) in anhydrous benzene (15 ml) under nitrogen was added a suspension of rhodium (II) acetate (10 mg) in anhydrous

benzene (5 ml). The reaction mixture was heated under reflux for 24 hr. The reaction mixture as filtered hot and dark brown crystals of the title compound (0.66 g; 2.2 mmol; 95%) precipitated out of the cooled benzene solution. Recrystallisation from dichloromethane/ether gave the title compound as cream crystals, m.p. 193-194°C.

Found: C, 43.75; H, 3.67; N, 4.75%. p^+:301.

$C_{11}H_{11}NO_7S$ requires: C, 43.85; H, 3.68; N, 4.65%. p^+:301.

N.m.r. (d^6-D.M.S.O.) δ_H 8.18 (1H, d, J = 6 Hz, olefinic proton), 7.28 (1H, d, J = 6 Hz, olefinic proton), 3.84 (3H, s, CO_2CH_3), 1.61 (6H, s, $C(CH_3)_2$), total integration correct.

I.r. ν_{max} 1780, 1685 (C=O) cm^{-1}.

3.9.11 Attempted decomposition of Meldrum's diazo in the presence of 3-isothiazolone

A solution of Meldrum's diazo (0.425 g; 2.5 mmol) and 3-isothiazolone (0.23 g; 2.3 mmol), together with a catalytic amount of rhodium (II) acetate, in anhydrous benzene (20 ml) was heated under reflux for 24 hr. T.l.c. was used to monitor the reaction and more catalyst was added after each sample was withdrawn because the diazo compound and the isothiazolone were still present. The now red reaction mixture was cooled and a red precipitate fell out of solution. The smell of acetic acid was evident. Filtration of the reaction mixture afforded red crystals which were heated under reflux in ether for 1 hr to remove organic impurities. The red crystals, m.p. 155°C dec., were too insoluble to obtain an n.m.r. spectrum but were thought to be $Rh_2(C_3H_2NOS)_4$ on the basis of i.r., mass spectral and analytical data.

Found: C, 26.29; H, 1.80; N,10.17%.

$C_{12}H_8N_4O_4Rh_2S_4$ requires: C, 23.77; H, 1.33; N, 9.24%.

A mass spectrum showed a peak at m/e 101.

I.r. ν_{max} 1630 (C=O) cm^{-1}.

The benzene solution contained only isothiazolone and diazo compound.

3.10 Reaction between arsonium ylides and activated olefins

3.10.1 Triphenylarsonium phenacylide and diethyl benzalmalonate

(i) In ethanol at room temperature

Triphenylarsonium phenacylide was generated in anhydrous ethanol (10 ml) at 0°C under nitrogen by the addition of sodium metal (0.078 g; 3.4 mmol) to a solution of phenacyltriphenylarsonium bromide (1.77 g; 3.5 mmol). After 15 min diethyl benzalmalonate (0.84 g; 3.4 mmol) in anhydrous ethanol (15 ml) was added dropwise. The reaction mixture was allowed to rise to room temperature overnight and the solvent was evaporated in vacuo to give an oil. This was triturated with dichloromethane and the filtrate was evaporated in vacuo to give a yellow oil (1.9 g). Trituration of this oil with ether gave a white solid which was identified as triphenylarsonium phenacylide (0.63 g; 42%) by spectroscopic comparison with an authentic sample.

(ii) In refluxing THF

A solution of triphenylarsonium phenacylide (1.0 g; 2.3 mmol) and diethyl benzalmalonate (0.57 g; 2.3 mmol) in anhydrous THF (10 ml) was heated under reflux for 60 hr under nitrogen. The solvent was removed in vacuo, the

resulting oil triturated with chloroform, and the filtrate evaporated to give an oil (1.8 g). Residual diethyl benzalmalonate was removed by bulb to bulb distillation (120°C; 0.5 mmHg) to leave an oil (1.4 g) which was chromatographed on 6% deactivated alumina (1"x8"). Elution with hexane gave triphenylarsine (0.5 g; 1.6 mmol ; 70%), identified by its n.m.r. Elution with ether removed two compounds together as an oil (0.62 g). Trituration with hexane afforded a white, fluffy solid which was identified as trans-1,2,3-tribenzoylcyclopropane (0.020 g; 0.06 mmol; 7.8%; p^+354), m.p. 215-217°C (lit.,[192] 219-220°C), and a brown oil (0.6 g) which was distilled (200°C; 0.5 mmHg) to give a yellow oil identified as trans-1-benzoyl-2,2-bis(carbethoxy)-3-phenylcyclopropane (0.3 g; 0.8 mmol; 35%).

(iii) In a melt

Triphenylarsonium phenacylide (0.4 g; 1 mmol) and diethyl benzalmalonate (1 ml) were heated together at 110°C for 2 hr and then left overnight at room temperature. Bulb to bulb distillation (120°C; 0.5 mmHg) of the reaction mixture gave a residual brown oil (0.49 g) and a distillate (0.69 g) which was shown by n.m.r. to contain diethyl benzalmalonate and a little triphenylarsine, but no cyclopropane derivative. The brown oil was chromatographed on 6% deactivated alumina (1" x 9"). Elution with hexane gave triphenylarsine (0.2 g; 0.65 mmol; 65%) identified by its i.r. Further elution with hexane gave trans-1-benzoyl-2,2-bis(carbethoxy)—3-phenylcyclopropane (0.15 g; 0.44 mmol; 44%). Bulb to bulb distillation (200°C; 0.5 mmHg) of this cyclopropane gave a pure sample (0.080 g; 0.22 mmol)

(lit.,[193] b.p. 198-200°C at 0.05 mmHg). The mass spectrum showed the correct parent ion p^+:366.

Found: 366.146867.

$C_{22}H_{22}O_5$ requires: 366.146713.

N.m.r. δ_H 8.2-8.0 (2H, c, aromatic protons), 7.6-7.1 (8H, c, aromatic protons), 4.4-3.8 (6H, c, methylene and ring protons), 1.3-0.9 (6H, 2t; t at 1.11 p.p.m., J = 8 Hz; t at 0.97 p.p.m., J = 6 Hz; $2CH_3$), total integration correct.

I.r. ν_{max} 1725 (br) (C=O), 1680 (C=O) cm^{-1}.

3.10.2 Stabilised arsonium ylides and diethyl ethoxymethylene-malonate

(i) With triphenylarsonium carbomethoxymethylide

Triphenylarsonium carbomethoxymethylide (0.4 g; 1.1 mmol) was heated in an excess of diethyl ethoxymethylene-malonate (1 ml) under nitrogen for 4 hr at 110°C. Trituration of the orange oil with ether afforded 3-carbomethoxy-1,1-dicarbethoxy-3-triphenylarsenanylprop-1-ene (0.34 g; 56.4%) which was crystallised from chloroform/hexane as colourless crystals, m.p. 197-198°C.

Found: C, 63.60; H, 5.18%.

$C_{29}H_{29}AsO_6$ requires: C, 63.51; H, 5.33%.

The mass spectrum showed the correct parent ion p^+:548.

Found: 548.119407.

$C_{29}H_{29}AsO_6$ requires: 548.118000.

N.m.r. δ_H 7.8-7.1 (16H, c, aromatic and methine protons, 4.03 (4H, q, J = 7 Hz, $2CH_2$), 3.41 (3H, s, OCH_3), 1.3-1.0 (6H, 2 x overlapping t, $CH_2\underline{CH}_3$), total integration correct.

I.r. ν_{max} 1670 (br) (C=O), 1640 (C=O) cm^{-1}.

(ii) With triphenylarsonium phenacylide

Triphenylarsonium phenacylide (0.5 g; 1.1 mmol) was heated in an excess of diethyl ethoxymethylenemalonate (1 ml) under nitrogen for 4 hr at 110°C. Addition of ether (10 ml) to the resulting red oil afforded yellow crystals (0.17 g; 26.4%) of 1,1-dicarbethoxy-4-oxo-4-phenyl-3-triphenylarsenanylbut-1-ene recrystallised from dichloromethane/ether as yellow needles, m.p. 192-192.5°C.

Found: C, 68.43; H, 5.22%.

$C_{34}H_{31}AsO_5$ requires: C, 68.69; H, 5.26%.

The mass spectrum showed the correct parent ion p^+:594.

Found: 594.138556

$C_{34}H_{31}AsO_5$ requires: 594.138735

N.m.r. δ_H 7.9-7.2 (21H, c, aromatic and methine protons), 3.97 (2H, q, J = 6 Hz, CH_2), 3.45 (2H, q, J = 6 Hz, CH_2). 1.2-0.9 (6H, 2 x overlapping t, CH_2CH_3), total integration correct.

I.r. ν_{max} 1700 (C=O), 1680 (C=O), 1660 (C=O) cm^{-1}.

T.l.c. of the leachings did not indicate any ylide.

3.11 Reaction between arsonium ylides and activated acetylenes

3.11.1 Methyl propiolate and triphenylarsonium phenacylide

(i) In benzene

A stirred solution of triphenylarsonium phenacylide (1.01 g; 2.5 mmol) and methyl propiolate (0.22 g; 2.5 mmol) in anhydrous benzene (20 ml) was heated under nitrogen at 50°C for 1 hr. The solvent was removed in vacuo and the residue (1.2 g) was chromatographed on 6% deactivated alumina (1.5" x 8"). Elution with ethyl acetate gave

2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene (0.57 g; 45%). Recrystallisation from dichloromethane/ether afforded the arsorane as yellow prisms, m.p. 184-185°C.

Found: C, 70.85; H, 4.94%.

$C_{30}H_{25}AsO_3$ requires: C, 70.86; H, 4.96%.

The mass spectrum showed the correct parent ion p^+:508.

Found: 508.100187.

$C_{30}H_{25}AsO_3$ requires: 508.101959

N.m.r. δ_H 8.1-7.1 (22H, c, aromatic and methine protons), 3.57 (3H, s, OCH_3), total integration correct. ^{13}C N.m.r. ($CDCl_3$) δ 188.05 (C=O), 167.68 (C-O), 146.23 (methine proton, J_{CH} = 4.84 Hz), 141-125 (aromatic), 105.79 (methine proton, J_{CH} = 4.93 Hz), 50.49 (methyl protons, J_{CH} = 2.97 Hz).

I.r. ν_{max} 1670 (C=O) cm^{-1}.

(ii) In methanol

A stirred solution of triphenylarsonium phenacylide (1.01 g; 2.5 mmol) and methyl propiolate (0.22 g; 2.5 mmol) in anhydrous methanol (20 ml) was heated under reflux under nitrogen for 3 hr. The solvent was removed in vacuo and the red oil (1.2 g) was triturated with ether to give trans-methyl 5-oxo-5-phenyl-4-triphenylarsenanylpent-2-enoate (0.67 g; 53%), recrystallised from chloroform/hexane as pale yellow prisms, m.p. 181-182°C dec.

Found: C, 70.77; H, 5.17%. p^+:508.

$C_{30}H_{25}AsO_3$ requires: C, 70.86; H, 4.96%. p^+:508.

N.m.r. δH 7.89 (1H, d, J = 15 Hz, olefinic proton), 7.7-7.3 (20H, c, aromatic protons), 4.42 (1H, d, J = 15 Hz, olefinic proton), 3.42 (3H, s, CH_3), total integration correct.

I.r. ν_{max} 1686 (C=O), 1586 (C=O) cm^{-1}.

3.11.2 d^1-Methyl propiolate and triphenylarsonium phenacylide

(i) In d^4-methanol

To a stirred solution of triphenylarsonium phenacylide (0.17 g; 0.4 mmol) in dry d^4-methanol (2 ml) at room temperature was added 71.5% d^1-methyl propiolate (0.034 g; 0.4 mmol in 0.040 g ether solution). Over 4 hr reflux the reaction mixture developed a deep red colouration. The solvent was evaporated in vacuo to afford a red oil (0.19 g) which was crystallised from chloroform/ether to give the bis-deuterated ylide in low yield (14.5%), m.p. 193.5-195°C.

The mass spectrum showed the correct parent ion p^+:510. N.m.r. δ_H 7.8-7.3 (20H, c, aromatic protons), 3.42 (3H, s, CH_3), total integration correct.

(ii) In methanol

In an identical experiment to that described above, the non-deuterated ylide was obtained.

(iii) In benzene

Partially deuterated arsorane was obtained by an identical procedure to that followed in 3.11.1(i).

3.11.3 Ethyl propiolate and triphenylarsonium phenacylide

The experimental procedure was as in 3.11.1.

(i) In benzene

2-Carbethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa-(V)cyclohexa-2,5-diene was obtained as an orange solid (50%), recrystallised from chloroform/hexane as yellow prisms, m.p. 169-169.5°C.

Found: C, 71.07; H, 5.17%. p^+:522.

$C_{31}H_{27}AsO_3$ requires: C, 71.26; H, 5.21%. p^+:522.

N.m.r. δ_H 7.95-7.15 (22H, c, aromatic and methine protons), 4.03 (2H, q, J = 7.4 Hz, CH_2), 0.92 (3H, t, J = 7.4 Hz, CH_3), total integration correct.
I.r. ν_{max} 1660 (C=O) cm^{-1}.

(ii) In ethanol

trans-Ethyl 5-oxo-5-phenyl-4-triphenylarsenanyl-pent-2-enoate was obtained as a yellow solid (78%), recrystallised from chloroform/ether as yellow needles, m.p. 167.5-168.5°C.

Found: C, 71.29; H, 5.14%. p^+:522.
$C_{31}H_{27}AsO_3$ requires: C, 71.26; H, 5.21%. p^+:5.22.
N.m.r. δ_H 7.86 (1H, d, J = 14.4 Hz, olefinic proton), 7.7-7.2 (20H, c, aromatic protons), 4.48 (1H, d, J = 14.4 Hz, olefinic proton), 3.89 (2H, q, J = 7.4 Hz, CH_2), 1.02 (3H, t, J = 7.4 Hz, CH_3), total integration correct.
I.r. ν_{max} 1680 (C=O), 1570 (C=O) cm^{-1}.

3.11.4 Methyl propiolate and triphenylphosphonium phenacylide

(i) In benzene

A solution of methyl propiolate (0.27 g; 3.3 mmol) and triphenylphosphonium phenacylide (1.25 g; 3.3 mmol) in anhydrous benzene (15 ml) was stirred at room temperature for 24 hr. The solvent was removed in vacuo and the resulting red oil (1 g) was triturated with ether to give trans-methyl 5-oxo-5-phenyl-4-triphenylphosphoranylpent-2-enoate (1.07 g; 70%) as a yellow powder. Recrystallisation from ethyl acetate gave yellow needles, m.p. 214-215°C.

Found: C, 77.59; H, 5.38%.
$C_{30}H_{25}O_3P$ requires: C, 77.57; H, 5.42%.

The mass spectrum showed the correct parent ion p^+:464.

Found: 464.1541.

$C_{30}H_{25}O_3P$ requires: 464.1534.

N.m.r. δ_H 7.9-7.2 (21H, c, aromatic and olefin protons), 4.49 (1H, d, J = 16 Hz, olefinic proton), 3.42 (3H, s, CH_3), total integration correct.

^{31}P N.m.r. ($CDCl_3$) δ 18.106.

I.r. ν_{max} 1685 (C=O), 1580 (C=O) cm^{-1}.

(ii) In methanol

In an identical experiment to that described above, trans-methyl 5-oxo-5-phenyl-4-triphenylphosphoranyl-pent-2-enoate was obtained as a yellow powder (58%). Recrystallisation from ethyl acetate gave yellow needles, m.p. 214-215°C.

Found: C, 77.57; H, 5.42%.

$C_{30}H_{25}O_3P$ requires: C, 77.69; H, 5.36%.

3.11.5 Propiolic esters with triphenylarsonium carbomethoxymethylide

(i) Methyl propiolate

A stirred solution of triphenylarsonium carbomethoxymethylide (0.4 g; 1.1 mmol) and methyl propiolate (0.1 g; 1.1 mmol) in anhydrous benzene (10 ml) under nitrogen was heated at 50°C for 5 hr. The solvent was removed in vacuo and the residual red oil (0.5 g) was chromatographed on 6% deactivated alumina (1.25" x 6"). Elution with dichloromethane afforded trans-dimethyl 4-triphenylarsenanylglutoconate as a yellow solid (0.3 g; 59%). Recrystallisation from hexane afforded yellow prisms, m.p. 152-153°C.

Found: C, 64.83; H, 5.15%.

$C_{25}H_{23}AsO_4$ requires: C, 64.94; H, 5.01%.

The mass spectrum showed the correct parent ion p^+:462.

Found: 462.084642

$C_{25}H_{23}AsO_4$ requires: 462.081224

N.m.r. δ_H 7.62 (15H, s, aromatic protons), 7.2 (1H, d, J = 14 Hz, olefinic proton), 5.92 (1H, d, J = 14 Hz, olefinic proton), 3.55 (6H, s, $2CH_3$), total integration correct.

I.r. ν_{max} 1680 (C=O), 1665 (C=O) cm^{-1}.

(ii) Ethyl propiolate

In an identical experiment to that described above, trans-1-carbethoxy-3-carbomethoxy-3-triphenylarsenanyl-prop-1-ene was obtained as a yellow powder (50%). Recrystallisation from chloroform/hexane afforded pale yellow prisms, m.p. 138.5-139°C.

Found: C, 65.27; H, 5.32%. p^+476.

$C_{26}H_{25}AsO_4$ requires: C, 65.55; H, 5.29%. p^+:476.

N.m.r. δ_H 7.53 (15H, s, aromatic protons), 7.22 (1H, d, J = 15 Hz, olefinic proton) 6.02 (1H, d, J = 15 Hz, olefinic proton), 4.01 (2H, q, J = 7 Hz, CH_2), 3.57 (3H, s, OCH_3), 0.98 (3H, t, J = 7 Hz, $CH_2\underline{CH_3}$), total integration correct.

I.r. ν_{max} 1684 (C=O), 1654 (C=O) cm^{-1}.

3.12 Reactions of propiolic ester-arsonium ylide adducts

3.12.1 Reaction of 2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene with dimethyl acetylene dicarboxylate

(i) 1:1 reaction mixture

A stirred solution of 2-carbomethoxy-4,4,4,6-

tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene (0.1 g; 0.2 mmol) and dimethyl acetylenedicarboxylate (0.031 g; 0.22 mmol) in anhydrous benzene (15 ml) under nitrogen was heated under reflux for 2 hr. The solvent was removed *in vacuo* and the residual red oil (0.13 g) was triturated with ether to give a residue which was washed with dichloromethane. The resulting white solid (63 mg) was identified as dimethyl 2-oxo-3-triphenylarsenanylsuccinate, m.p. 206-208°C (lit.,[50] 214°C).

N.m.r. δ_H 7.7-7.1 (15H, *c*, aromatic protons), 3.84 (3H, *s*, CO_2CH_3), 3.3 (3H, *s*, CO_2CH_3), total integration correct.

I.r. ν_{max} 1742, 1675, 1550 cm^{-1}.

The trituration leachings were evaporated to yield a red oil (0.1 g). Preparative t.l.c. afforded 2,4,5-triscarbomethoxybiphenyl (30 mg) which was identical to that obtained below, and some were ylide (10 mg).

(ii) *1:2 reaction mixture*

A stirred solution of 2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene (0.322 g; 0.63 mmol) and dimethyl acetylenedicarboxylate (0.18 g; 1.3 mmol) in anhydrous benzene (15 ml) under nitrogen was heated under reflux for 5 hr. The solvent was removed *in vacuo* and the residual oil (0.5 g) was triturated with ether to give dimethyl 2-oxo-3-triphenylarsenanylsuccinate as a white powder (0.24 g) which was recrystallised from ethyl acetate, m.p. 210-211°C (lit.,[50] 214°C). The trituration leachings were evaporated *in vacuo* (<10^{-3} mmHg to remove acetylene) to give a red oil (0.262 g) which was recrystallised from ether to give colourless prisms of 2,4,5-triscarbomethoxy-

biphenyl, m.p. 131-131.5°C.

Found: C, 65.91; H, 4.90%.

$C_{18}H_{16}O_6$ requires: C, 65.85; H, 4.91%.

The mass spectrum showed the correct parent ion p^+:328.

Found: 328.094022.

$C_{18}H_{16}O_6$ requires: 328.094679.

N.m.r. ($CDCl_3$) δ_H 8.21 (1H, s, aromatic proton), 7.67 (1H, s, aromatic proton), 7.5-7.3 (5H, c, aromatic proton), 3.91 and 3.93 (3H each, s, $2CO_2CH_3$), 3.67 (3H, s, CO_2CH_3), total integration correct.

I.r. ν_{max}, 1748 (C=O), 1735 (C=O), 1722 (C=O) cm^{-1}.

3.12.2 Attempted reaction of 2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene with methyl propiolate

A stirred solution of triphenylarsonium phenacylide (0.52 g; 1.23 mmol) and methyl propiolate (0.31 g; 3.69 mmol) in benzene (15 ml) was heated under reflux under nitrogen for 2 hr after stirring at room temperature for 12 hr. The reaction mixture was evaporated in vacuo and triturated with ether to give 2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa-(V)cyclohexa-2,5-diene as yellow crystals (0.387 g; 62%), m.p. 180-181°C identical to that obtained in section 3.11.

3.12.3 Reaction of deuterated 2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene with dimethyl acetylenedicarboxylate

Partially deuterated arsorane (0.337 g), proposed by reaction of 95% d^1-methyl propiolate with triphenylarsonium phenacylide, and dimethyl acetylenedicarboxylate (0.18 g;

1.26 mmol) in benzene (15 ml) were stirred under reflux under nitrogen for 2 hr. The reaction mixture was evaporated *in vacuo* and the residual red oil (0.51 g). Trituration of this oil with ether, followed by evaporation of the leachings afforded an oil (0.21 g) which was recrystallised from ether, m.p. 119.5-122°C. The mass spectrum showed the correct parent ion p^+: N.m.r. ($CDCl_3$) δ_H 8.21 (0.5H, s), 7.67 (1H, s).

3.12.4 *Attempted rearrangement of 2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene*

The title arsorane (0.1 g; 0.2 mmol) was heated under reflux in methanol (15 ml) for 5 hr. T.l.c. indicated that only the arsorane was present and no reaction had occurred. The solvent was removed *in vacuo* to afford a yellow solid which was triturated with ether to give the arsorane (0.095 g) unchanged.

3.12.5 *Pyrolysis of 2-carbomethoxy-4,4,4,6-tetraphenyl-1,4-oxarsa(V)cyclohexa-2,5-diene*

The arsorane (0.3 g; 0.59 mmol) was heated on a Kugelrohr at 200°C and 0.5 mmHg for 20 hr. The distillate (0.21 g) was chromatographed preparative t.l.c. on alumina (1:1 hexane-ether as eluant) to afford triphenylarsine (0.15 g; 0.49 g). No other products were observed.

3.12.6 Pyrolysis of trans-methyl 5-oxo-5-phenyl-4-triphenyl arsenanylpent-2-enoate

The ylide (58.6 mg; 0.11 mmol) was heated under flash vapour conditions (<0.001 mmHg; furnace 500°C; inlet oven 200°C) to afford triphenylarsine (10.9 mg; 0.03 mmol) as the sublimate. Unreacted ylide (8.2 mg; 0.02 mmol) was recovered in the inlet tube. No other products were observed.

3.13 Reaction of ethyldiphenylarsonium benzylide with benzaldehyde

The same experimental procedure was used irrespective whether benzene, ether, THF or DME was employed as solvent.

n-Butyllithium (1.0 ml; 1.0 M in hexane) was added to a stirred suspension of benzylethyldiphenylarsonium bromide (0.429 g; 1 mmol) in anhydrous solvent (25 ml) under a nitrogen atmosphere. To the resulting orange coloured solution, benzaldehyde (0.106 g; 1 mmol)* was added** and, after a further interval***, the reaction mixtures were heated under reflux for 2 hr. The solution was then made up to 50 ml with chloroform and analysed by glc using p-methylstilbene or cis-stilbene as the internal standard.

* The benzaldehyde was purified by stirring overnight with sodium carbonate, followed by vacuum distillation under N_2 from a pinch of zinc dust. The reagent was protected from aerial oxidation and maintained under a dry nitrogen atmosphere in the dark at all times.

Solvent	Internal Standard	Trans-Stilbene	Cis-Stilbene	Trans-Stilbene Oxide	Cis-Stilbene Oxide	Epoxide/Olefin
THF	a	23.4	-	35.0	-	1.49
	b	24.8	-	39.3	-	1.58
DME	b	13.02		47.10	-	3.62
	b	9.54	-	38.01	-	3.98
Ether	b	7.46	2.65	14.15	-	1.40
Benzene	b	4.42	-	30.79	-	6.97
Theoretical plates		1822.89	1601.06	1447.94		
Plate height/cm		0.109	0.125	0.138		

a - cis-stilbene

b - p-methylstilbene

Percentage products for ylide/benzaldehyde reaction.

Table 11

** The interval was 30 min (THF, DME) or 5 min (ether, benzene). This was because the colour of the benzene and ether solutions became less intense during the 30 min interval following addition of the base, indicating that thermal decomposition had occurred.

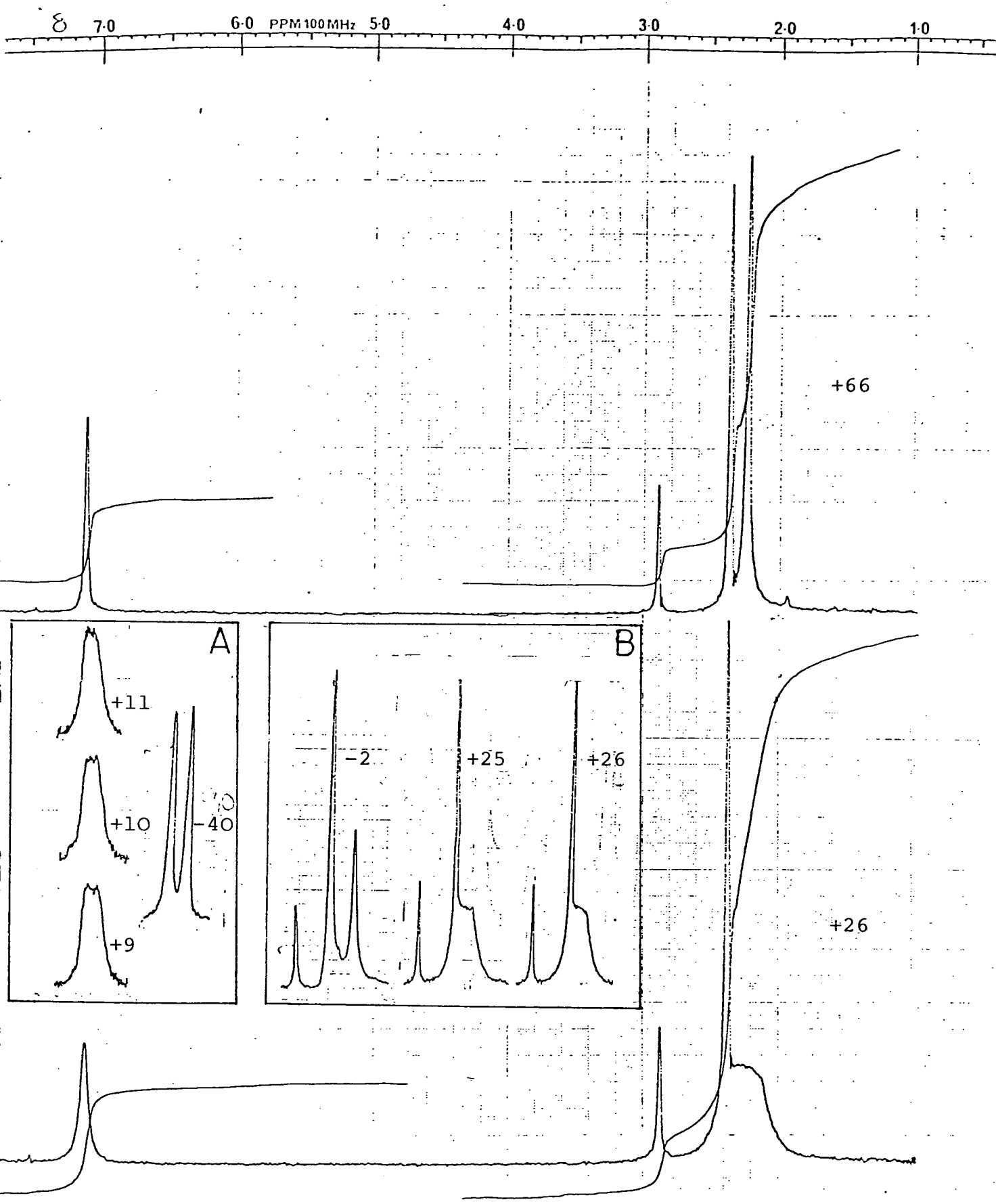
*** THF, DME - 24 hr
Ether, benzene - 15 min.

The components of the reaction mixtures were eluted in the following order:

cis-stilbene, ethyldiphenylarsine, trans-stilbene, and trans-stilbene oxide.

The internal standard p-methylstilbene was eluted last.

The results are presented in Table 11.



Inset A meta-protons Inset B Me-protons

Figure A. Variable temperature ^{1}H n.m.r. spectra for methyltrimesitylarsonium iodide.

Appendix

Restricted rotation in arsonium salts, a n.m.r. spectroscopic study

1. Discussion

In the last ten years there has been considerable interest in the dynamic stereochemistry of molecular propellers[194], the work of Mislow and his group[194,195] on systems Ar_3Z and Ar_3ZX e.g. Mes_3CH (Mes = 2,4,6-trimethylphenyl)[196] being particularly prominent. As part of a ^1H n.m.r. study into such systems conducted by A.J. Bellamy (Department of Chemistry, Edinburgh), it was found necessary to prepare trimesitylarsine and tris(2,4,6-trimethoxyphenyl)arsine together with their methiodides. The arsines were prepared by the method of Stepanov and co-workers[197]. Both arsines were colourless crystalline solids purified by recrystallisation. Their methiodides were prepared by heating with methyl iodide under reflux for five hours.

The temperature at which coalescence of the two singlets for the diastereotopic ortho-methyl groups, and for the diastereotopic meta-hydrogen atom occurs was measured for methyltrimesitylarsonium iodide (see Figure A). However, no coalescence was observed for methyltris(2,4,6-trimethoxyphenyl)arsonium iodide in deuteriochloroform (see Figure B).

In order to calculate the rate constant for enantiomerisation (k_{en}) it was assumed that the

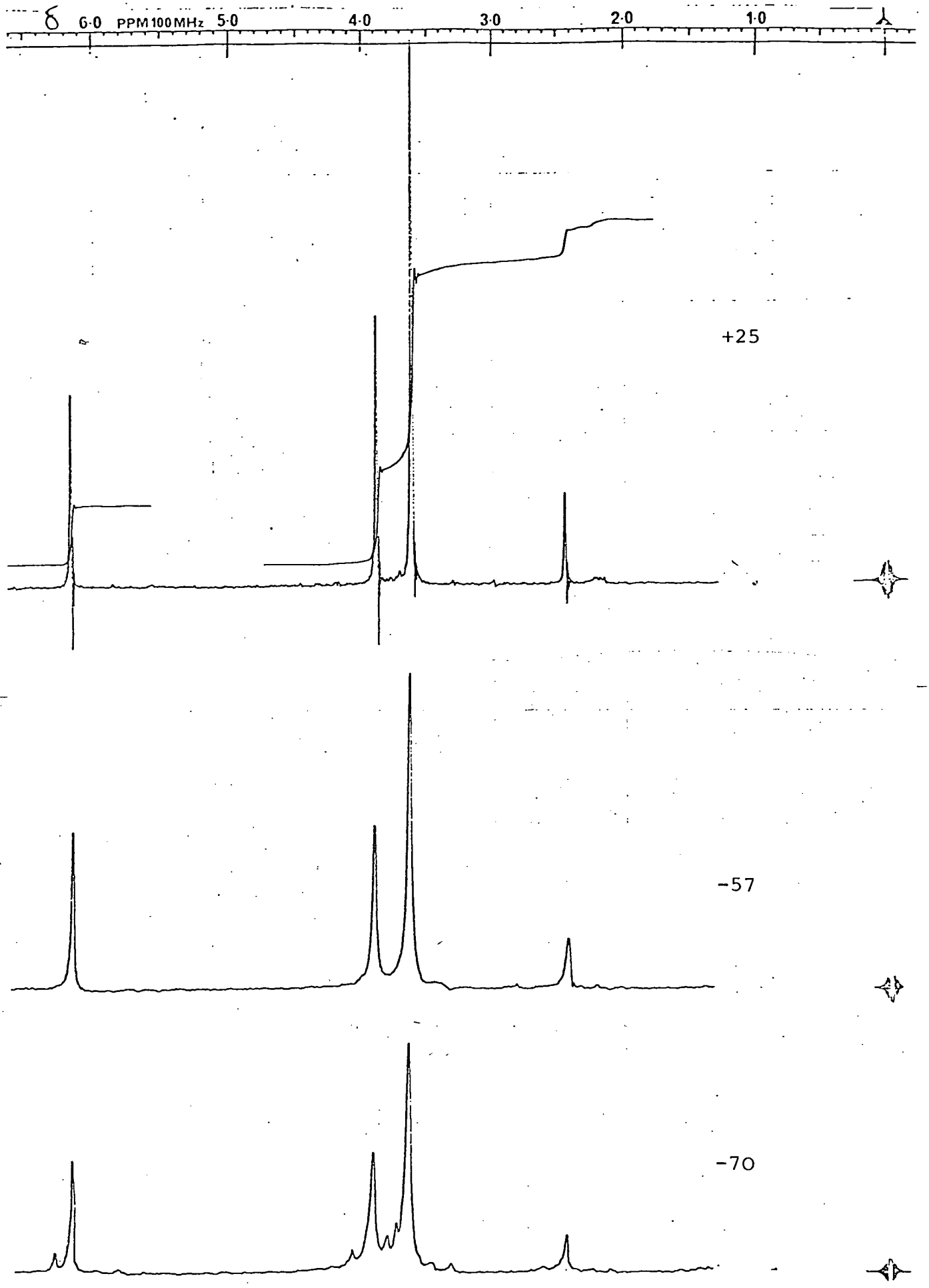


Figure B. Variable temperature ^{1}H n.m.r. spectra for methyltris(2,4,6-trimethoxyphenyl)arsonium iodide.

methyltrimesitylarsonium iodide system produces signal averaging by three consecutive two-ring flip processes as shown by Mislow and co-workers to occur for Mes_3CH[196]. The coalescence temperature gives $k_{coalescence}$ (k_c), which is the overall rate constant for three consecutive steps. Since only one two-ring flip is required to enantiomerise the helicity of the molecular propeller (the threshold mechanism), $k_{en} = 3 \times k_c$. The activation energy for enantiomerisation, $\Delta G^{\ddagger}_{T_c}$, (the threshold barrier) at the coalescence temperature was calculated from k_{en}. There is good agreement between the $\Delta G^{\ddagger}_{T_c}$ values calculated from both the ortho-methyl signals (14.2 k cal mol^{-1}) and the meta-hydrogen signals (14.0 k cal mol^{-1}), although the former are considered to be more accurate due to the larger $\Delta\nu$ involved. For completeness, the results of other workers for similar propellers are included in the Table.

Empirical force field calculations on Mes_3CH have revealed that in the transition state for the two-ring flip mechanism, the most severe non-bonded interactions are between the pairs of proximal and distal ortho-methyl groups of the flipping rings, and their associated ring carbon atoms, and between the ortho-methyl groups of the non-flipping ring and the carbon atoms attached to the central atom in the flipping rings[196a]. Any lengthening of the bonds between the rings and the central atom should relieve these interactions and thus lower the energy of the transition state. The general trend observed for $\Delta G^{\ddagger}_{T_c}$:

$$Mes_3CH > Mes_3P^{+}CH_3 > Mes_3As^{+}CH_3 > Mes_3P > Mes_3As$$

Table Coalescence temperatures and $\Delta G^{\ddagger}$ values for some Mes_3ZX systems

Compound (solvent)	$\Delta\nu_{\underline{o}\text{-Me}}$ /Hz	T_c (o-Me) /°C	k_{en}[a] /s^{-1}	$\Delta G^{\ddagger}_{T_c}$[b] /k cal mol^{-1}	$\Delta\nu_{\underline{m}\text{-H}}$ /Hz	Tc (m-H) /°C	k_{en}[a] /s^{-1}	$\Delta G^{\ddagger}_{Tc}$[b] /k cal mol^{-1}
Mes_3CH (C_4Cl_6)[196a]	17	167	113	21.9				
$Mes_3P(CDCl_3)$[198]	44	-38	293	11.0	13	-53	87	10.8
$Mes_3\overset{+}{P}CH_3BF_4^-$ (DMSO-d_6)[198]	40	91	266	17.4	18	78	120	17.3
$Mes_3\overset{+}{P}CH_2CN\ I^-$ (DMSO-d_6)[198]	46	113	306	18.4	17	97	113	18.3
Mes_3As (CS_2)[198]		-101		8.8				
$Mes_3\overset{+}{As}CH_3\ I^-$ ($CDCl_3$)	37	25	246	14.2	13	10	87	14.0

a: $k_{en} = k_{enantiomerisation} = 3 \times k_{coalescence}$ (assumes two-ring flip mechanism, see ref 196a).

$k_{coalescence} = \pi\Delta\nu/\sqrt{2}$

b: $\Delta G^{\ddagger}$ for enantiomerisation $= -RT_c \ln \frac{k_{en}}{T_c} \frac{h}{k}$

can be largely attributed to such a lengthening of the central bonds. The central bonds in representative members of the series are: 1.54 Å for Mes_3CH[199], 1.84 Å for Mes_3P[200], and 1.99 Å for $(2,5\text{-}Me_2C_6H_4)_3As$[201]. The differences between the phosphine and the phosphonium cation, and between the arsine and the arsonium cation, can be attributed to the extra non-bonded interactions between the proximal ortho-methyl groups in the two flipping rings and the introduced group, with the introduction of a fourth group (CH_3) having a larger effect ($\Delta\Delta G^{\ddagger}_{T_c}$ = 6.4 k cal mol^{-1} for $Mes_3P \rightarrow Mes_3P^+CH_3$, and 5.4 k cal mol^{-1} for $Mes_3As \rightarrow Mes_3As^+CH_3$) than changing the central atom, and hence the central bond length ($\Delta\Delta G^{\ddagger}_{T_c}$ = 2.2 k cal mol^{-1} for $Mes_3As \rightarrow Mes_3P$, and 3.2 k cal mol^{-1} for $Mes_3As^+CH_3 \rightarrow Mes_3P^+CH_3$).

2. Experimental

Trimesitylarsine Mesityl magnesium bromide was generated from bromomesitylene (15.92 g; 80 mmol) and magnesium (1.94 g; 80 mmol) in anhydrous THF (45 ml). To the cooled solution of the Grignard was added arsenic trichloride (3.73 g; 20.6 mmol) in THF (10 ml) and the mixture was heated under reflux for 2 hr. The reaction mixture was then cooled, aqueous ammonium chloride solution added, followed by extraction into benzene. The organic layer was separated, washed with dilute aqueous sodium hydroxide solution followed by water. Evaporation in vacuo afforded a white residue which was suspended in ethanol and filtered to give trimesitylarsine (6.6 g; 75%) recrystallised from hexane-ethanol as colourless

crystals,

m.p. 167.5-169°C (lit[16] 170°C).

N.m.r. δ_H 6.74 (6H, s, meta-H), 2.21 (9H, s, para-CH_3), 2.12 (18H, s, ortho-CH_3), total integration correct.

^{13}C N.m.r. ($CDCl_3$) δ 142.71 (As-C), 137.27 (C-CH_3), 135.81 (C-CH_3), 129.43 (meta-C), 22.98 (ortho-CH_3), 20.71 (para-CH_3).

Tris(2,4,6-trimethoxyphenyl)arsine This compound (4.6 g; 78%) was prepared as for trimesitylarsine from 2,4,6-trimethoxyphenylbromide (9.9 g; 40 mmol), magnesium (0.97 g; 40 mmol) and arsenic trichloride (1.9 g; 10.3 mmol) as colourless crystals (from ether), m.p. 163-164°C.

Methyltrimesitylarsonium iodide A solution of trimesitylarsine (1.08 g; 2.5 mmol) in methyl iodide (16 ml) was heated under reflux under nitrogen for 5 hr. The cooled solution was filtered to afford methyltrimesitylarsonium iodide (1.21 g; 84%), recrystallised from ethanol-water and then ethanol-hexane as yellow crystals, m.p. 195-197°C.

Found: C, 58.63; H, 6.42%.

$C_{28}H_{36}AsI$ requires: C, 58.54; H, 6.32%.

N.m.r. (+66°C) δ_H 7.07 (6H, s, meta-H, T_c = 10°C, $\Delta\nu$ = 13 Hz (-42°C)), 2.87 (3H, s, As-CH_3), 2.34 (9H, s, para-CH_3), 2.21 (18H, s, ortho-CH_3, T_c = 25°C, $\Delta\nu$ = 36.5 Hz (-42°C)), total integration correct.

^{13}C N.m.r. ($CDCl_3$) δ 143.29 (C-CH_3), 140.69 (C-CH_3), 131.84 (meta-C), 125.16 (As-C), 25.08 (As-CH_3), 22.75 (ortho-CH_3), 20.29 (para-CH_3).

I.r. ν_{max} 1602, 1290, 905, 870, 860, 734 cm^{-1}.

Methyltris(2,4,6-trimethoxyphenyl)arsonium iodide

Tris(2,4,6-trimethoxyphenyl)arsine (1.44 g; 2.5 mmol) was heated under reflux in methyl iodide (20 ml) for 5 hr. Hexane was added to precipitate a gum, the mother liquors were decanted, and the gum was triturated with more hexane to afforded a yellow powder (1.73 g; 96%), recrystallised from ethanol-hexane as orange needles, m.p. 203-204°C.

Found: C, 47.08; H, 5.33%.

$C_{28}H_{36}AsIO_9$ requires: C, 46.80; H, 5.05%.

N.m.r. δ_H 6.17 (6H, s, meta-H, T_c < -70°C), 3.89 (9H, s, para-OCH_3), 3.62 (18H, s, ortho-OCH_3), 2.48 (3H, s, As-CH_3), total integration correct.

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