THE REACTIONS OF TRIVALENT PHOSPHORUS COMPOUNDS WITH ELECTROPHILIC ACETYLENES

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by

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Julian Caesar

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TO MY PARENTS

'The most beautiful thing
one can experience is the
mysterious. It is the
source of all time, art,
and science .....'

Albert Einstein.

Abstract

This thesis is concerned with the investigation of the reactions of some trivalent phosphorus compounds with electrophilic acetylenes, and in particular dimethyl acetylenedicarboxylate. These studies have involved extensive use of nuclear magnetic resonance (n.m.r.) spectroscopy to monitor reaction pathways and to identify intermediates.

The nature of the 1:1 intermediate initially formed in the reaction of a trivalent phosphorus compound, such as a trialkyl phosphite, with dimethyl acetylenedicarboxylate has been studied and shown to exhibit both anionic and carbenoid character.

The reaction of these 1:1 intermediates with further dimethyl acetylenedicarboxylate leads to the formation of unstable ylides which rearrange at room temperature to cyclic ylides via five-coordinate phosphoranes. Both these latter two species have been shown to be valuable precursors for the preparation of some novel oxo-phospholes.

The 1:1 intermediates from trialkyl phosphites react with carbon dioxide to form "CO_2-adducts" which react with further trialkyl phosphite to give ylides. These ylides have been shown to provide convenient synthetic routes to some phosphonates and substituted furans which would otherwise be difficult to prepare. The progress of the carbon dioxide in these reaction pathways has been investigated by ^{13}C n.m.r. spectroscopy, by using ^{13}C isotopically labelled carbon dioxide.

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INTRODUCTION

INTRODUCTION

The Reaction of Trivalent Phosphorus Compounds with Electrophilic Acetylenes.

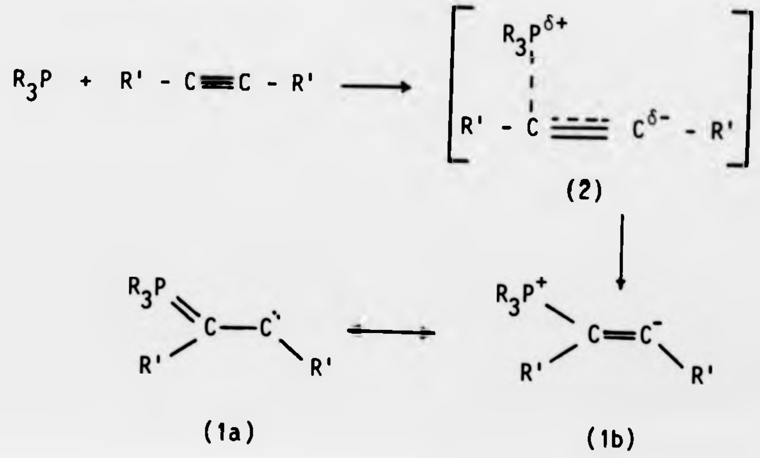
Trivalent phosphorus compounds can behave as nucleophiles by virtue of the lone pair of electrons on the phosphorus. They are, in fact, more powerful nucleophiles than their nitrogen analogues due to the lower electronegativity and greater polarisability of the trivalent phosphorus atom. They therefore react readily either at unsaturated centres, such as carbonyl groups or carbon-carbon double and triple bonds, or by displacement of a leaving group, such as a halide at a saturated carbon atom. (Fig. 1).

$$PCl_3 + 3RCOOH \longrightarrow RCOCl + (HO)_2PHO$$

$$Ph_3P + PhCH_2Br \longrightarrow Ph_3\overset{+}{P}CH_2Ph\ Br^-$$

Fig. 1

Although the reaction of trivalent phosphorus compounds with electrophilic acetylenes can give rise to a wide range of products their formation can be rationalised as proceeding via the initially formed 1:1 intermediate (1).



It has been suggested[1] that the formation of this 1:1 intermediate (1) is facilitated by pπ-dπ bonding which not only lowers the energy of the transition state (2), by reinforcing the incipient σ bond, but also stabilizes the initially formed betaine (1b). The eventual products from the reaction depend on the subsequent reactions of this 1:1 intermediate (1).

It is convenient to subdivide the reactions of the trivalent phosphorus compounds with electrophilic acetylenes on the basis of the nature of the products formed. Thus, for example those reactions leading to the formation of a product which arises from the reaction of two trivalent phosphorus centres with a single carbon-carbon triple bond will be considered under the general heading of "2:1 ADDUCTS". It should be noted however, that since some of the reactants to be considered contain more than one reactive centre, e.g. diphosphines, the adduct ratio does not necessarily represent the molar ratio of the reactants.

1. "2:1 ADDUCTS"

1.1 Reactions involving dialkyl acetylenedicarboxylates.

(i) Triphenylphosphine

The reaction of dimethyl acetylenedicarboxylate with an excess of triphenylphosphine was first investigated by Johnson and Tebby[2] who tentatively identified the product as a 2:1 adduct, the alkylidene-1,2-diphosphorane (3), on the basis of analytical evidence. Thus, for example, the 2:1 adduct showed a band arising from the carbonyl group at 1592 cm^{-1} which is characteristic of stable alkylidenephosphoranes.[3] It has been suggested that the low value of this absorption band indicates that the zwitterionic structures (3a, 3b, and 3c) must make a major contribution to the overall structure.[4]

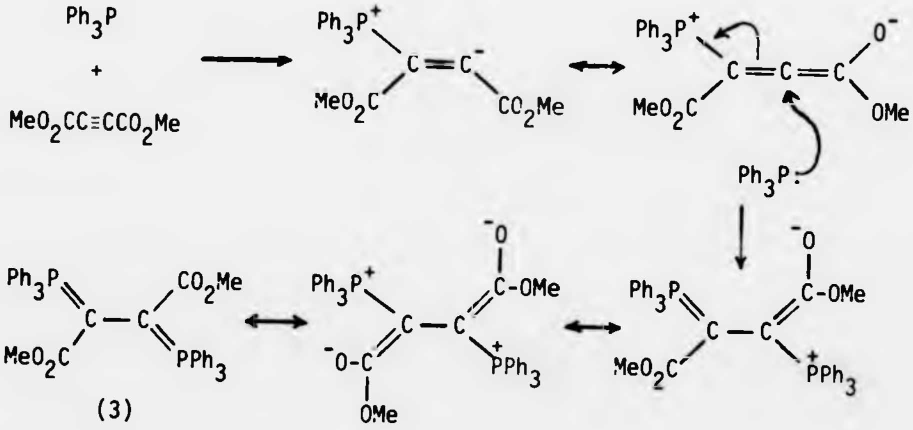
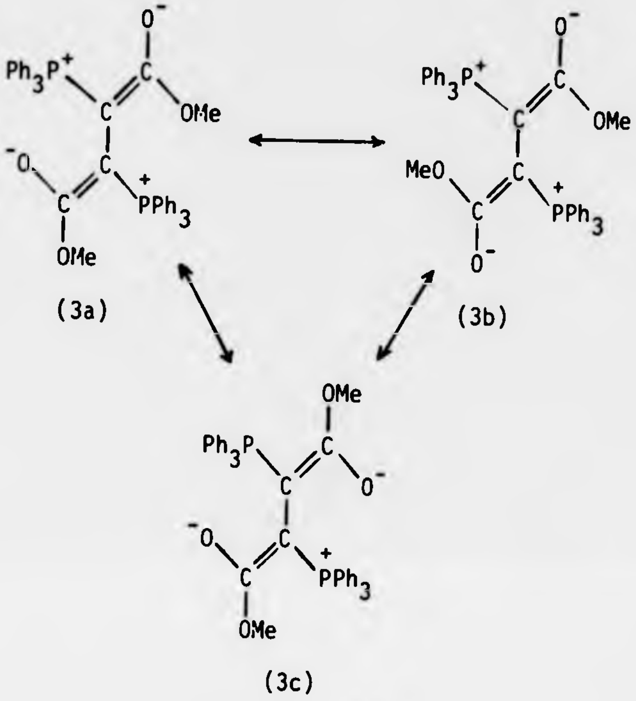


Fig. 2



(3a) (3b) (3c)

The adduct (3) was later shown by ^1H n.m.r. spectroscopy to exist as the three slowly-interconverting conformers (3a, 3b, and 3c) at low temperature.[4] This type of behaviour at low temperature is a characteristic feature of alkylidenephosphoranes containing the α-alkoxycarbonyl group[5,6] and is due to the restricted rotation about the bond to the α-methoxycarbonyl group arising from the partial double-bond character in that bond. The molecular formula of (3) has also been confirmed by mass spectroscopy, with reductive cleavage and hydrolysis providing further support for the assigned structure.[4,7,8] Thus, reductive cleavage with zinc and acetic acid gave triphenylphosphine and dimethyl succinate while hydrolysis gave triphenylphosphine, triphenylphosphine oxide and dimethyl fumarate. The concerted mechanism shown in Fig. 3 has been proposed for the hydrolysis of (3). The earlier proposal that the mechanism proceeded via the phosphoranyl-phosphonium salt (4) is less satisfactory since it is now thought that this salt would be too stable to undergo spontaneous fragmentation.[8]

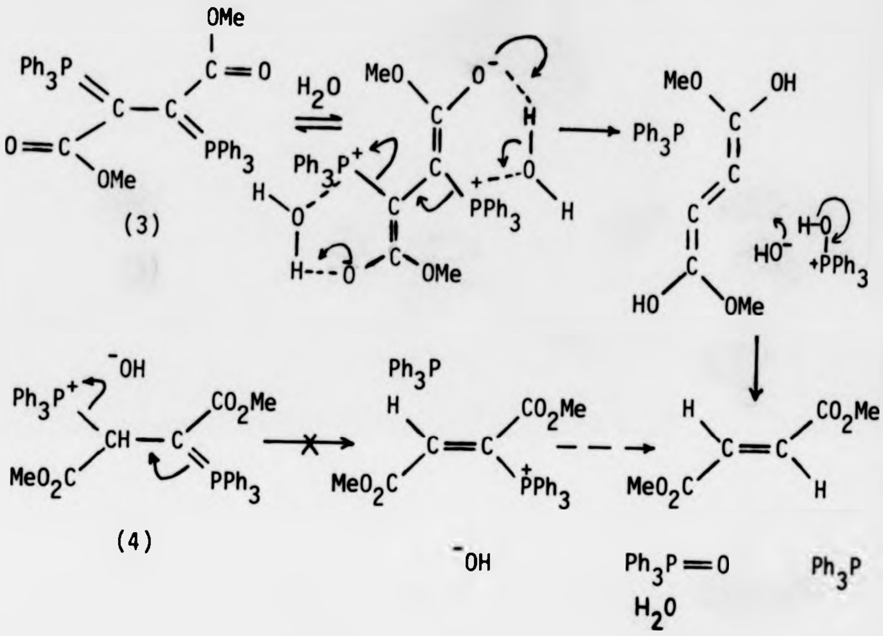


Fig. 3

(ii) Bis(diphenylphosphino)methane.

In the reaction of bis(diphenylphosphino)methane with dimethyl acetylenedicarboxylate (Fig. 4) an intramolecular reaction leading to a cyclic 2:1 adduct occurred.[7] However, the infra-red and n.m.r. spectra of this material indicated that the product was not the expected alkylidene phosphorane (5) but its tautomeric form (6), a diphosphole. Thus, for example, the infra-red spectrum of the 2:1 adduct showed strong absorption bands at both 1737 and 1620 cm^{-1} indicating the presence of both non-conjugated and conjugated carbonyl groups. Furthermore, the ^1H n.m.r. spectrum showed two single proton resonances at δ5.00 and 1.25 p.p.m., the latter being assigned to the protons on the carbon bridging the two phosphorus atoms.[7] In addition, the spectrum was temperature dependent as expected for an alkylidene phosphorane possessing an α-alkoxycarbonyl group, and showed the presence of two conformers at low temperature as a result of the restricted rotation about the bond to the α-alkoxycarbonyl group.

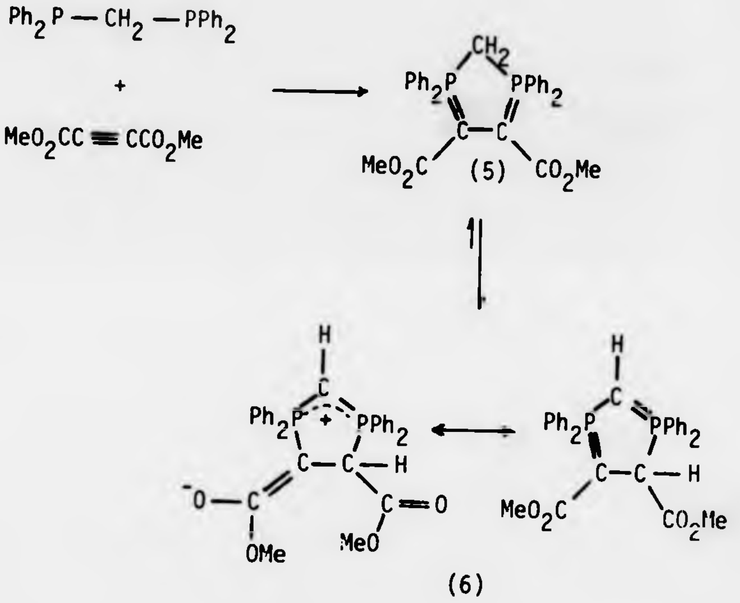


Fig. 4

(iii) Bis(diphenylphosphino)ethane.

Hughes and Jafry[9] have prepared 1,4-diphosphacyclohexa-1,3-diene (7) by the reaction of bis(diphenylphosphino)ethane with dimethyl acetylenedicarboxylate. (Fig. 5).

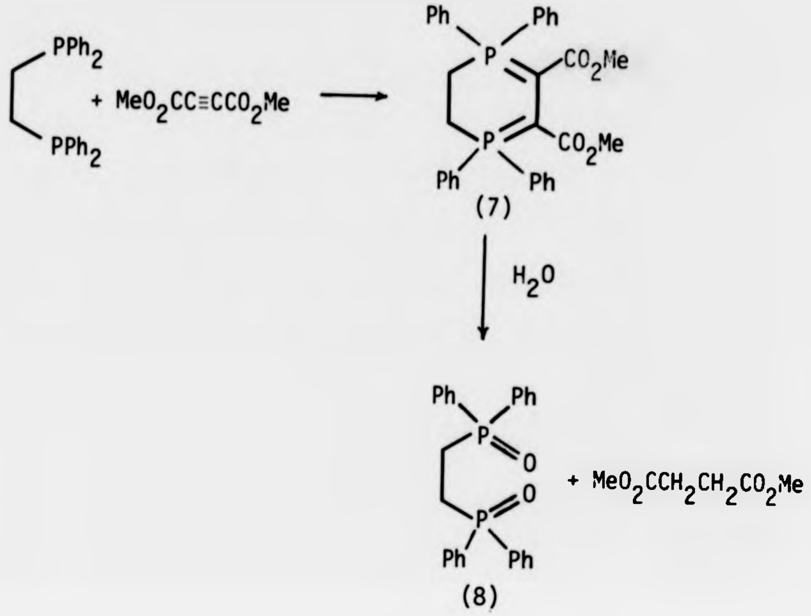


Fig. 5

Evidence for this structure was obtained from the observation that on hydrolysis the diphosphorane (7) gave the bis(diphenylphosphino)ethane dioxide (8). The mechanism of formation of the 1,4-diphosphacyclohexa-1,3-diene (7) is believed to involve a number of intramolecular steps and is closely related to that proposed for the preparation of other 1,2-diphosphoranes such as (3). The proposed mechanism for the formation of the diphosphorane (7) is shown in Fig. 6, although it should be noted that a slightly different mechanism had originally been proposed on the basis of other related reactions.[9,10]

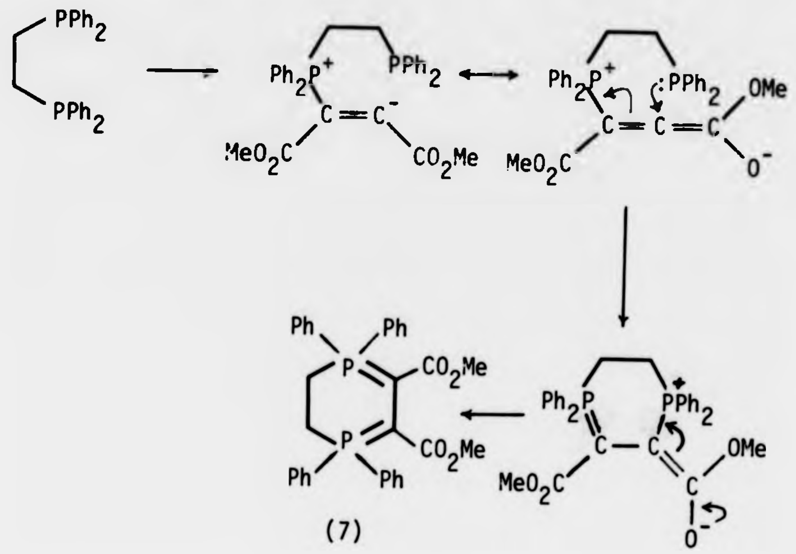
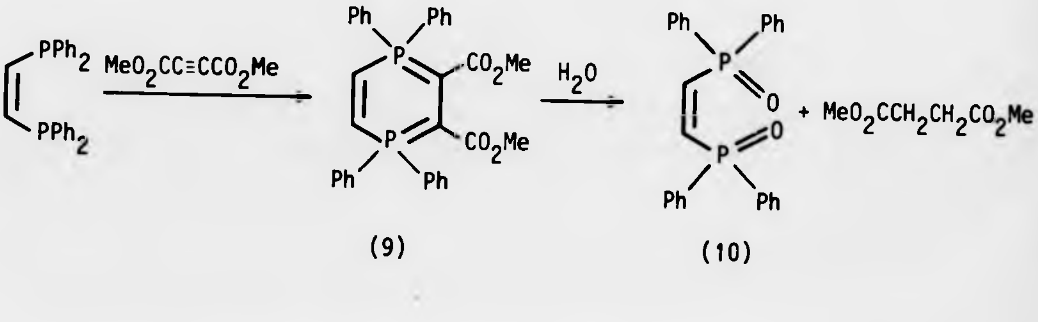


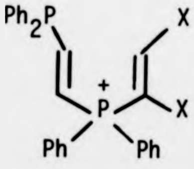
Fig. 6

(iv) *cis*-1,2-Bis(diphenylphosphino)ethylene

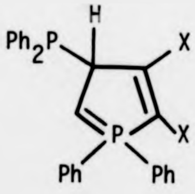
cis-1,2-Bis(diphenylphosphino)ethylene reacts with an equimolar quantity of dimethyl acetylenedicarboxylate to produce the unstable 1,4-diphosphorin derivative (9).[7]



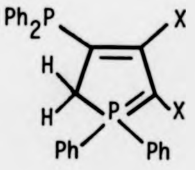
Unfortunately, the instability of this adduct precluded its complete characterisation although its infra-red and mass spectra were consistent with the proposed structure. The rapid hydrolysis of (9) even in air to give *cis*-1,2-bis(diphenylphosphino)ethylene dioxide (10) and dimethyl succinate has prevented useful n.m.r. data being obtained. The reaction of *trans*-1,2-bis(diphenylphosphino)-ethylene with dimethyl acetylenedicarboxylate has also been investigated.[11] However, instead of the formation of a 1,4-diphosphorin a highly water sensitive adduct was obtained. The n.m.r. spectrum of this material was interpreted as indicating that the adduct existed largely as (11a) although possibly in tautomeric equilibrium with the ylidic structures (11b), (11c), and (11d).



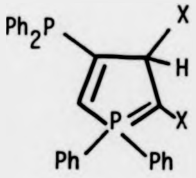
(11a)



(11b)



(11c)



(11d)

The behaviour of this adduct towards hydrolysis was found to be interesting since the product (12) was also formed in the hydrolysis of the dihydrophosphole (13). It has therefore been suggested that the hydrolysis of the adduct (11a) proceeds via the dihydrophosphole (13).[11] (see Fig. 7).

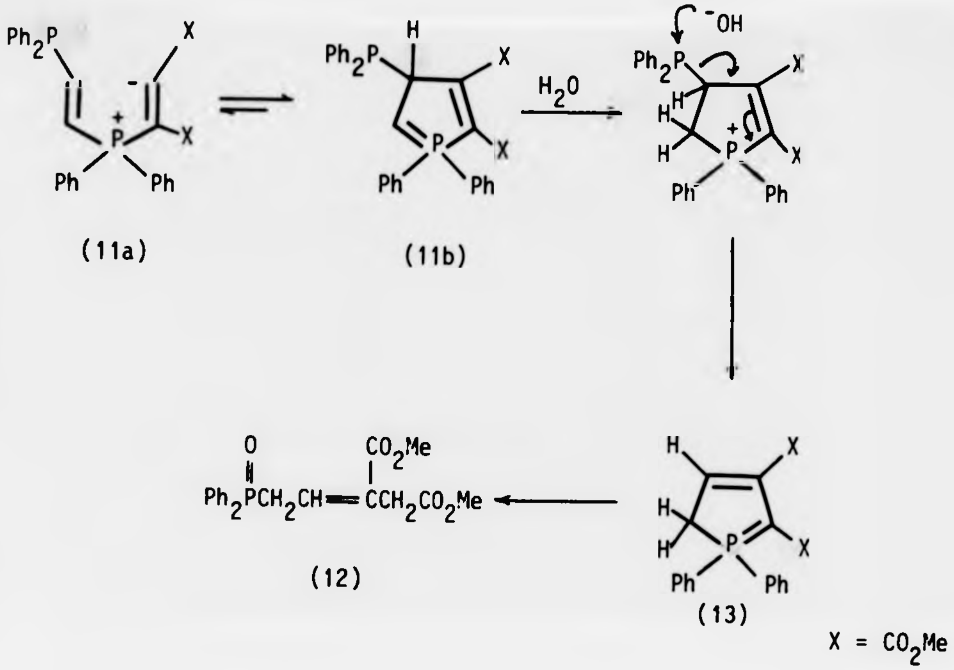
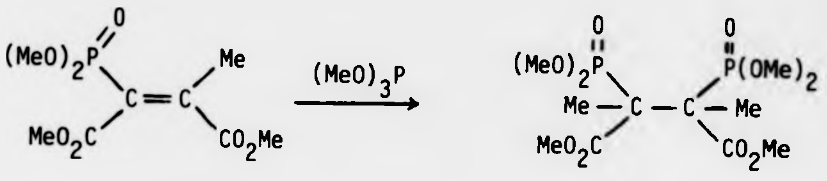


Fig. 7

(v) Trimethyl phosphite

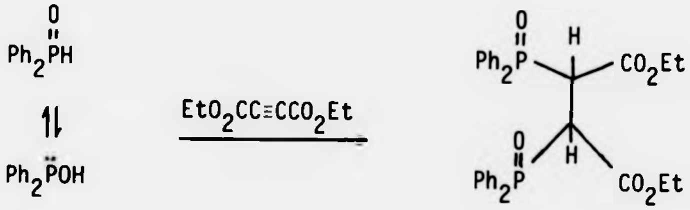
The reaction of trimethyl phosphite with dimethyl acetylenedicarboxylate has also been investigated. Griffin and Mitchell[12] reported the formation of a 2:1 adduct from the reaction of DMAD with a two molar equivalent of trimethyl phosphite. The product isolated from the reaction by distillation was shown to be the diphosphonate (14), which they proposed as resulting from the attack by trimethyl phosphite on an initially formed vinyl phosphonate (15).


(15) (14)

Our work in this area indicates that this is not the case [see later discussion].

(vi) Diphenylphosphine oxide.

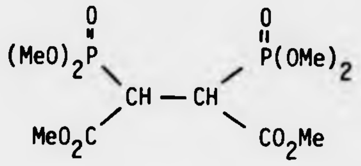
Diphenylphosphine oxide has been shown to react with diethyl acetylenedicarboxylate to give the 2:1 adduct (16)[13] in the absence of base.


(16)

It has been proposed that this reaction involves the diphenylphosphine oxide attacking the acetylene as its trivalent tautomer.

(vii) Dimethyl phosphite

Although dimethyl phosphite is not strictly a trivalent phosphorus compound, it is worth noting that this material reacts with dimethyl acetylenedicarboxylate in an analogous manner to that observed with diphenylphosphine oxide, to give the diphosphonate (17).[14]



(17)

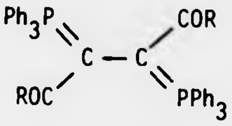
(viii) Other phosphines.

1,2-Diphosphoranes analogous to (3) have also been prepared by the reaction of, for example, diphenylmethylphosphine,[4] tri-p-chlorophenylphosphine,[15] and diphenylchlorophosphine[16] with dimethyl acetylenedicarboxylate.

1.2 Reactions involving diaroyl acetylenes.

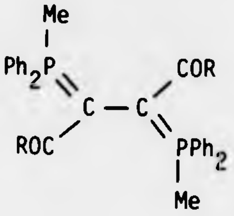
(i) Triphenylphosphine and diphenylmethylphosphine.

The diaroyl-1,2-diphosphoranes (18a), (18b), (19a), and (19b) have been prepared by the reaction of excess triphenylphosphine or diphenylmethylphosphine with dibenzoyl- or di-p-toluoylacetylenes in ether.[8]



(18a) R = Ph

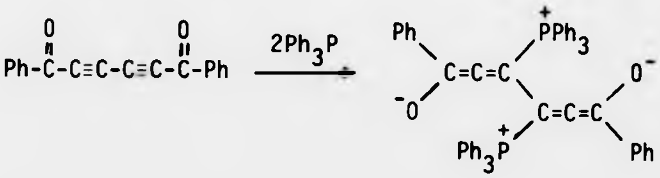
(18b) R = p-tolyl



(19a) R = Ph

(19b) R = p-tolyl

These diphosphoranes were much less stable than those from dimethyl acetylenedicarboxylate and readily hydrolysed. The reaction of tri-p-toluoylphosphine and tri-p-methoxyphenylphosphine with dibenzoylacetylene[15] produced stable diaroyl-1,2-diphosphoranes analogous to (18). Horner and Hoffmann[17] have referred to the claim that (20) is formed by the reaction of two moles of triphenylphosphine with dibenzoyldiacetylene.

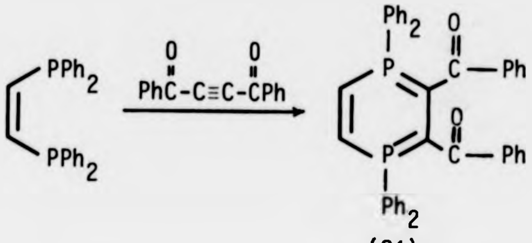


(20)

However, it was noted that further work would be needed to confirm this.

(ii) cis-1,2-Bis(diphenylphosphino)ethylene.

The reaction of cis-1,2-bis(diphenylphosphino)ethylene with dibenzoylacetylene has been found to be analogous to the reaction with dimethyl acetylenedicarboxylate previously discussed, the product being an unstable 1,4-diphosphorin (21).[7]



(21)

Once again, the instability of this material prevented complete characterisation.

1.3 Reactions involving less electrophilic acetylenes.

(i) Trialkyl phosphite.

In order to induce a reaction between a trialkyl phosphite and a non-activated acetylene such as phenylacetylene it is necessary to use more vigorous conditions. Thus, the reaction of triethylphosphite (2 moles) with phenylacetylene (1 mole) required some 36h at a temperature of 150 °C. Under these conditions a small quantity (6%) of the phosphonate (22)[18] was isolated together with an intractable tar. The proposed mechanism of the formation of the diphosphonate (22) is shown in Fig. 8.

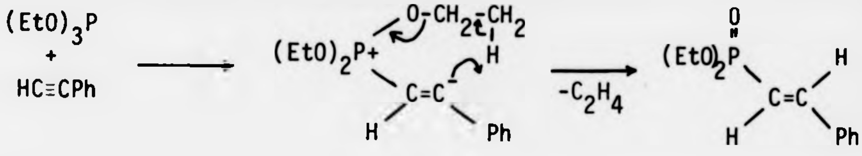
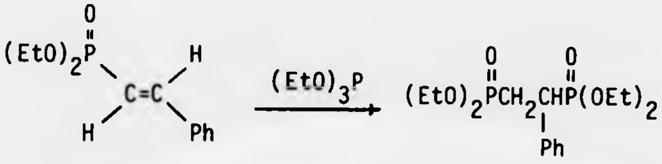


Fig. 8

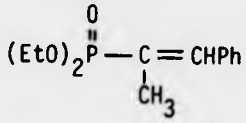
(22)

In the presence of a large excess of triethyl phosphite (12:1) the reaction proceeded to give 1,2-bis(diethylphosphono)-1-phenylethane (23) (16.7%)[18] which was shown to arise from the reaction of the phosphonate (22) with triethyl phosphite.


(22)

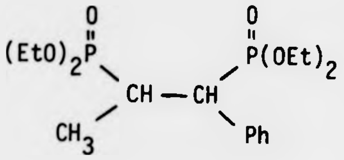
(23)

The corresponding reaction between methyl phenylacetylene[18] and triethyl phosphite gave the phosphonate (24) in 23% yield and the diphosphonate (25) in 11% yield after 9 days at 150 °C.



$(EtO)_2P(O){-}C(CH_3){=}CHPh$

(24)



(25)

Alkyl acetylenes are even less reactive than aryl acetylenes. Pudovik[19] has shown that tertiary acetylenic chlorides (26) react with trialkyl phosphites to give bisphosphonates (27) as the final product, but this involves an initial Arbusov reaction with displacement of the chloride ion to give the allenyl phosphonate (28) rather than direct reaction at the carbon-carbon triple bond (Fig. 9).

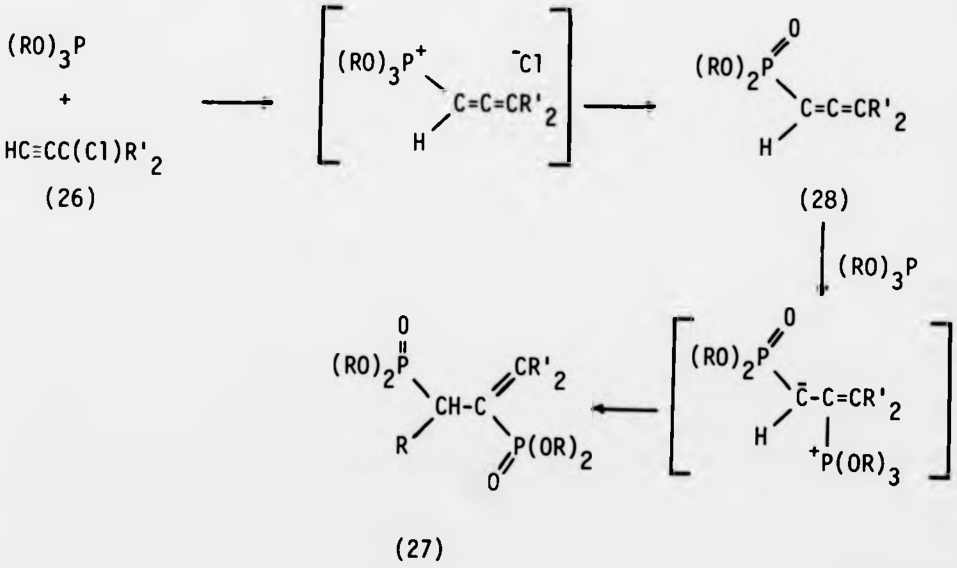
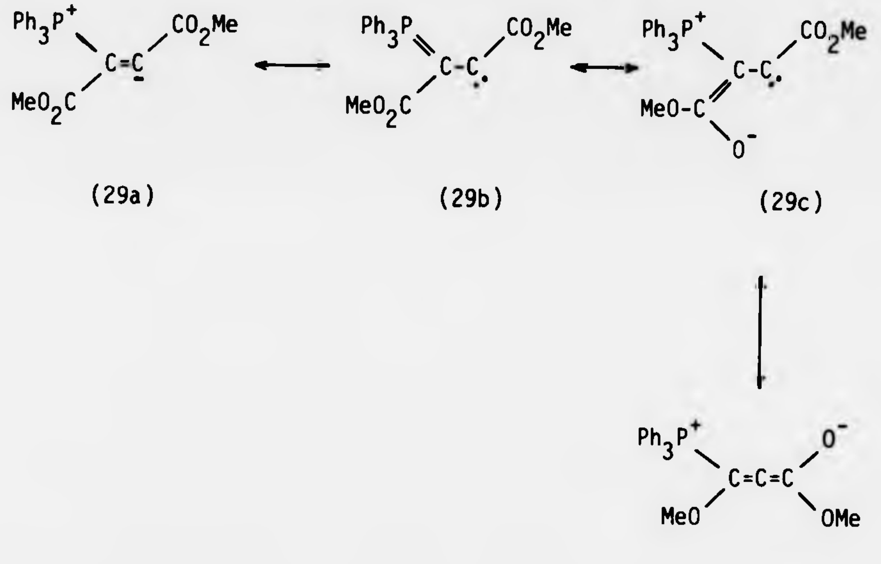


Fig. 9

2. "1:1 ADDUCTS AND PRODUCTS DERIVED AS A RESULT OF TRAPPING UNSTABLE 1:1 INTERMEDIATES."

2.1 1:1 Intermediates.

Horner and Hoffman[17] have claimed to have isolated the 1:1 intermediate formed in the reaction of triphenylphosphine with dimethyl acetylenedicarboxylate. The structure proposed was that of (29d), one of the number of possible canonical forms.



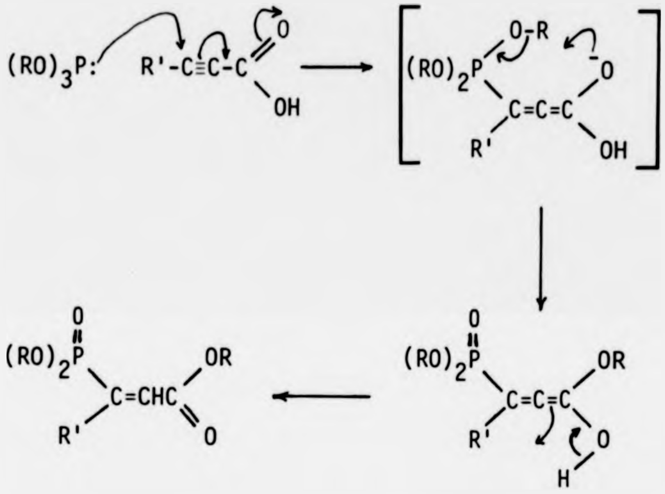
(29a) (29b) (29c)

(29d)

It should be noted however, that other workers have been unable to isolate a 1:1 intermediate from this reaction although they have been able to trap it by the addition of appropriate compounds to the reaction mixture.[2,15]

2.2 Rearrangement of a 1:1 intermediate.

Trialkyl phosphites react with acetylenic acids to give β-alkoxycarbonylvinyl phosphonates (30)[20] by rearrangement of the initially formed 1:1 intermediate.



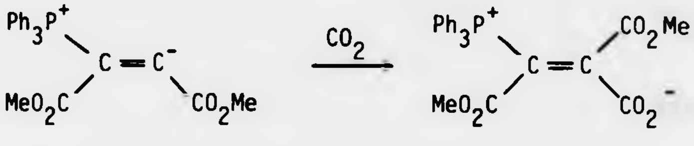
(30)

The formation of the β-alkoxycarbonylvinyl phosphonates (30) can be viewed as an intramolecular trapping of the initially formed 1:1 intermediate in the absence of additional trapping compounds.

2.3 Reactions of 1:1 intermediates.

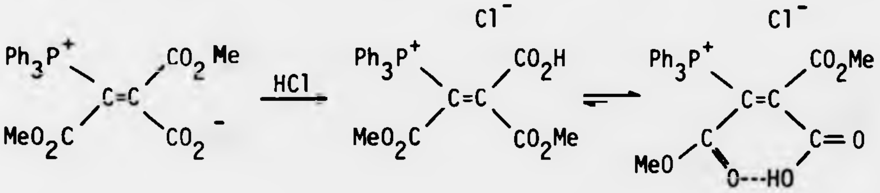
(i) Carbon Dioxide.

Johnson and Tebby,[2] obtained the colourless betaine (31) at -50 °C, when the generation of the 1:1 adduct (29a) was carried out in the presence of carbon dioxide.



(29a) (31)

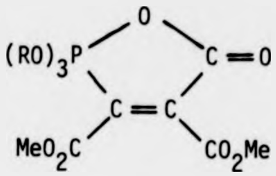
Protonation of the carboxylate betaine (31) with anhydrous hydrogen chloride is claimed to give a mixture of two phosphonium salts (32a) and (32b), with the trans isomer (32b) predominating.[21] Thus, the hydrolysis of either this mixture of phosphonium salts (32), or the original carboxylate betaine (31), gave triphenylphosphine oxide and a mixture of dimethyl fumarate and dimethyl maleate in a 3:1 ratio.



(31) (32a) (32b)

Griffiths and Tebby[22] have also investigated the reaction of trialkyl phosphite with dimethyl acetylenedicarboxylate in the presence of carbon dioxide. As with the reaction involving triphenylphosphine, the phosphite reaction led to the formation of an adduct with carbon dioxide, although this adduct was shown to be the cyclic phosphorane

(33) rather than the ionic structure such as that proposed for the carboxylate betaine (31).

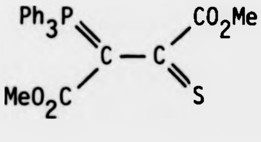


(33)

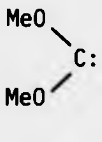
The reactivity of the cyclic phosphorane (33) towards additional trialkyl phosphite led to an additional side reaction [see later discussion] which prevented it from being prepared and isolated in a pure form.

(ii) Sulphur

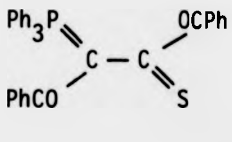
The 1:1 intermediate from the reaction of triphenylphosphine and dimethyl acetylenedicarboxylate (29) has also been trapped by the addition of elemental sulphur to the reaction mixture.[15] It has been suggested that the nature of the product (34) the thioketone, 1,2-dimethoxycarbonyl-2-thioxoethylidenetriphenylphosphorane, reflects the contribution made to the structure of (29) by the canonical form (29b) which is a carbene. The reaction with elemental sulphur to give a thioketone is known to be characteristic of nucleophilic carbenes such as dimethoxycarbene (32).[23]



(34)



(35)

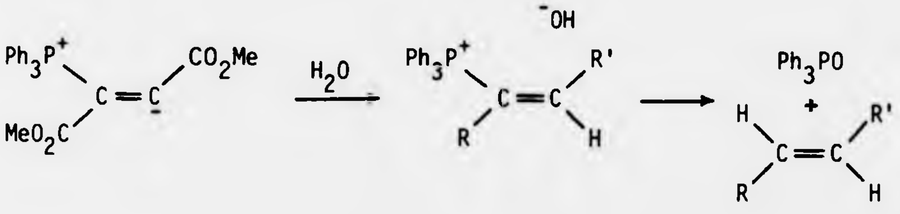


(36)

The analogous thioketone (36)[15] has also been prepared from the reaction of triphenylphosphine with dibenzoylacetylene in the presence of sulphur. The carboxylate betaine (31) has also proved to be a good source of the 1:1 intermediate (29) so that decomposition of the carboxylate betaine (31) in the presence of elemental sulphur was found to be a convenient route to the formation of (31).[15]

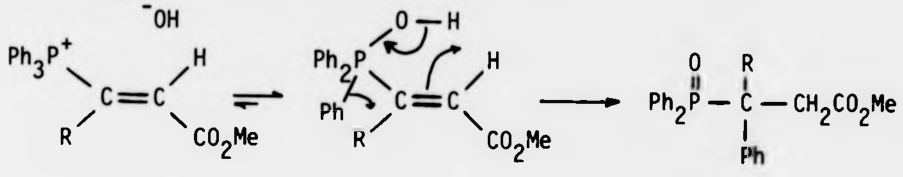
(iii) Water.

When the 1:1 intermediate (29) is generated from triphenylphosphine and dimethyl acetylenedicarboxylate in the presence of water protonation of the intermediate occurs. This is followed by fragmentation of the vinylphosphonium hydroxide (37; R,R'=CO_2Me) to give triphenylphosphine oxide and dimethyl fumarate. This route for the preparation of alkenes has been extended to other electrophilic acetylenes and provides a convenient means of incorporating deuterium selectively at the carbon-carbon double bond.[24,25]



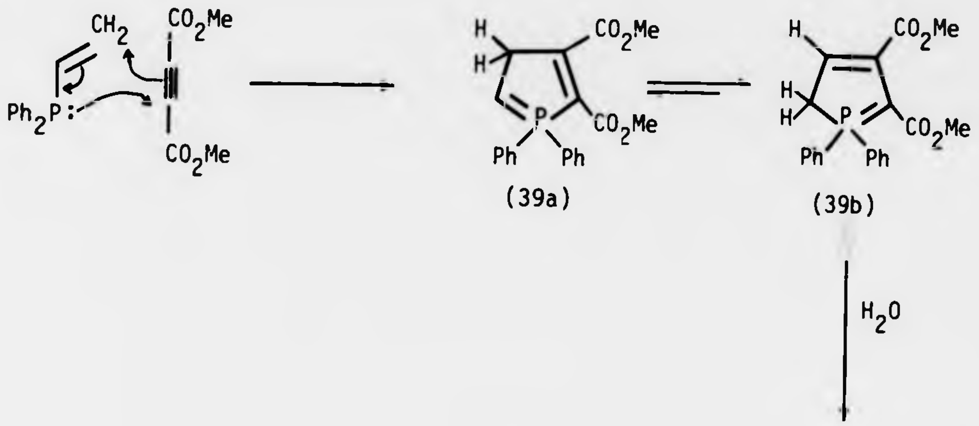
(29) (37)

The disubstituted acetylenes, dimethylacetylenedicarboxylate, diphenyl and dibenzoylacetylene, reacted with triphenylphosphine in the presence of water to give mainly the trans-alkenes in yields of 40-70%. With deuterium oxide similar yields of the corresponding 1,2-dideuterio alkenes were obtained. In those cases where the intermediate (37) possessed an electron-withdrawing group on the α-carbon the hydrolytic cleavage of the phosphonium salt was promoted. However, vinylphosphonium hydroxides formed from the reaction of triphenylphosphine with monosubstituted electrophilic acetylenes and water, e.g. (37; R=H, Me) rearrange to phosphine oxides (38; R=H, Me) by an aryl migration from the phosphorus atom to the adjacent α-carbon of the aliphatic chain.[26,27]



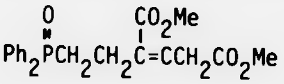
(37) R=H, Me (38)

When dimethyl acetylenedicarboxylate was added to diphenylvinylphosphine in the presence of water the cycloadduct (39) was formed which was isolated as the hydrolysis product (12).[11] The reaction was found to be dependent on the ratio of the reactants and the reverse addition of the vinylphosphine to the acetylenic ester led to the formation of other products [see Fig. 7]. This has been interpreted as indicating that the cycloaddition product is a mixture of two highly reactive dihydrophosphole tautomers (39a) and (39b),[11] with (39b) being the more stable.



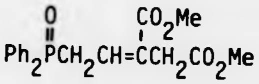
(39a)

(39b)



$Ph_2\overset{O}{\overset{\|}{P}}CH_2CH_2\overset{CO_2Me}{\overset{|}{C}}=CCH_2CO_2Me$

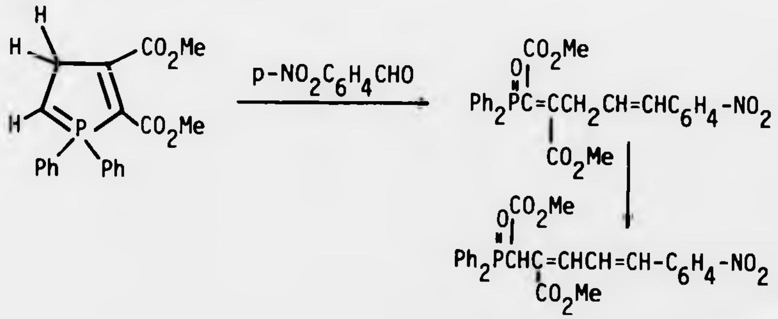
(40)



$Ph_2\overset{O}{\overset{\|}{P}}CH_2CH=\overset{CO_2Me}{\overset{|}{C}}CH_2CO_2Me$

(12)

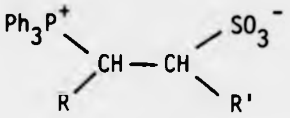
Although hydrolysis of (39a) might be expected to give the phosphine oxide (40) none was formed in the reaction. The dihydrophosphole (39a) could, however, be trapped by the addition of p-nitrobenzaldehyde to give the phosphine oxide (41).[11,28]



(41)

(iv) Sulphur dioxide/water.

Triphenylphosphoniaethane sulphonates (42) are formed when the reaction of triphenylphosphine with an electrophilic acetylene is carried out in the presence of sulphur dioxide and water.[25,29]



(42)

The reaction is believed to proceed via an attack by the bisulphite ion (formed from sulphur dioxide and water) with the initially formed α,β-unsaturated phosphonium hydroxide as shown in Fig. 10. The sulphonate betaine (42) fragmented on heating but formed a stable alkylidenephosphorane (43) on treatment with alkali.[29] The slow interconversion of the threo and erythro form of (42) in solution demonstrates the lability of the α-methine proton in this system.

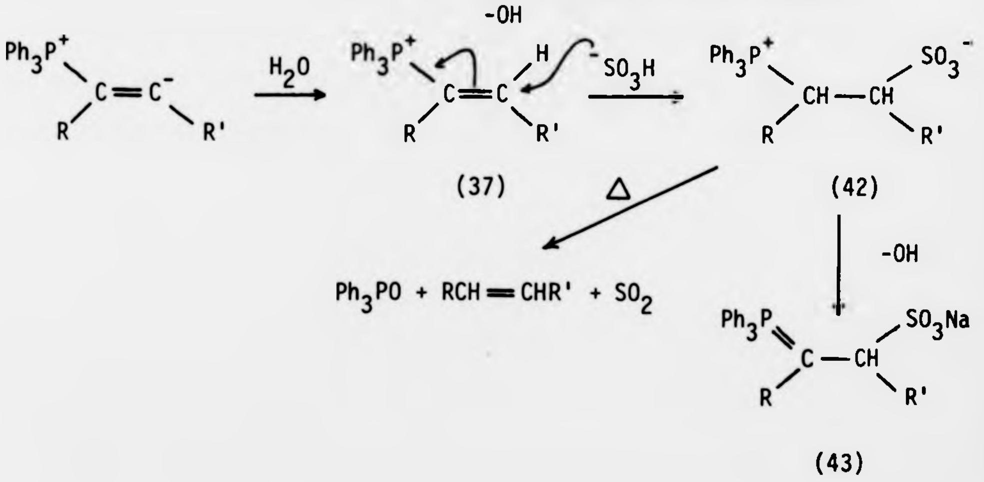
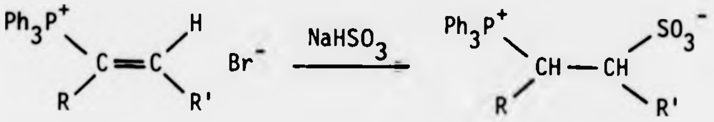


Fig. 10

The sulphonate betaines (42; $R,R'=CO_2Me$) and (42; $R'=CO_2Me$, R=H) have also been synthesised from the appropriate vinylphosphonium bromide (44) by the action of sodium bisulphite. The vinylphosphonium bromides are prepared by trapping the 1:1 intermediate formed from the reaction of triphenylphosphine with the appropriate acetylene in the presence of hydrogen bromide.[29,30]



(44) (42)

(v) Alcohols (+ phenol and carboxylic acids).

Wilson and Tebby[31] have studied the reaction of triphenylphosphine with acetylenic esters in alcoholic media and have shown that either stable β-alkoxyvinylphosphonium ylides (45) or vinyl ethers (46) are formed. (Fig. 11). The latter arise from the alcoholysis of the vinylphosphonium intermediate (47), which occurs in the reaction of propiolate esters where no stable β-alkoxyvinylphosphonium ylide can be formed.

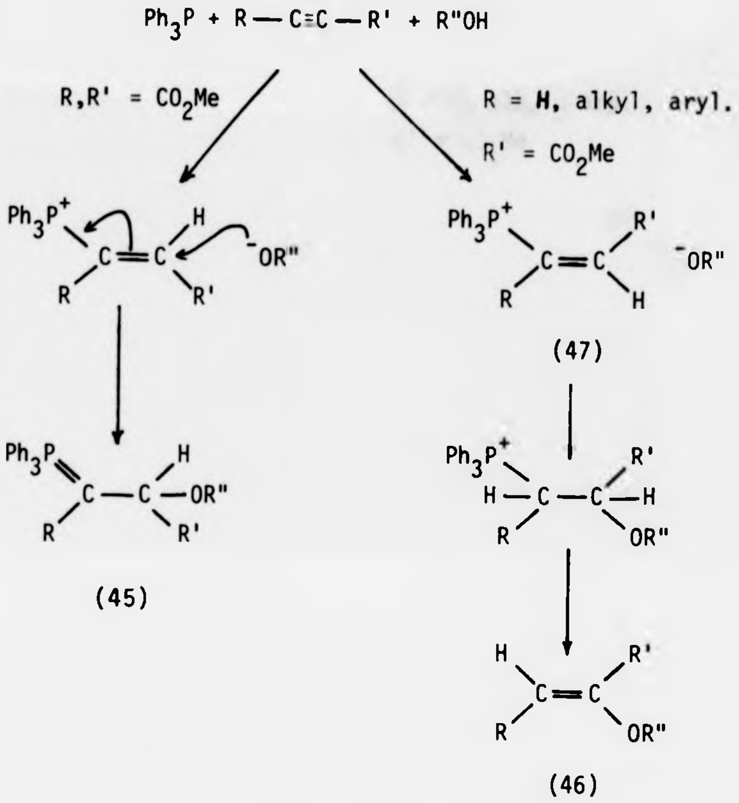
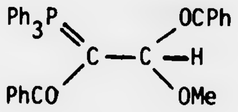


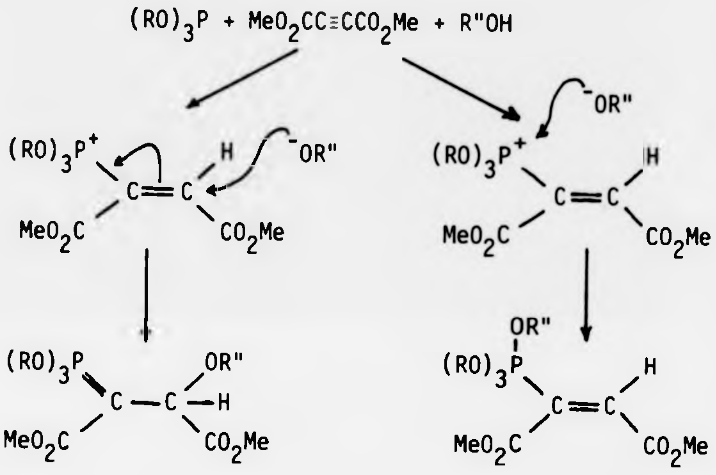
Fig. 11

The reaction of triphenylphosphine with dibenzoylacetylene in methanol occurred in a similar manner to give the phosphorane (48).[31]



(48)

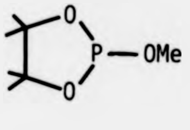
Burgada's group[32-36] studied the analogous reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate in alcoholic media. They too found that the initially formed 1:1 intermediate could be conveniently trapped by protic reagents, but that the reaction subsequently followed one of two possible routes. The first, leading to a phosphonium ylide (49) is analogous to the triphenylphosphine reaction.



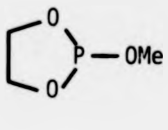
(49) (50)

Fig. 12

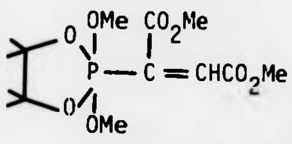
However, an alternative route involving reaction at the phosphorus atom, was also observed leading to the formation of a five-coordinate phosphorane (50). When the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate in methanol was extended to the cyclic phosphites (51),[32-37] the corresponding five coordinate phosphorane (52) was produced in almost quantitative yield.



(51a)

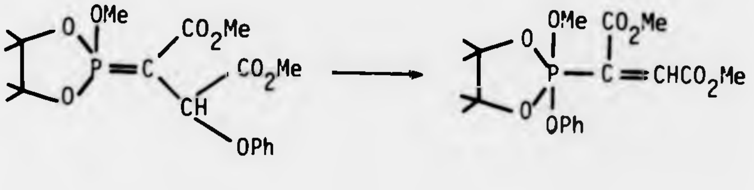


(51b)



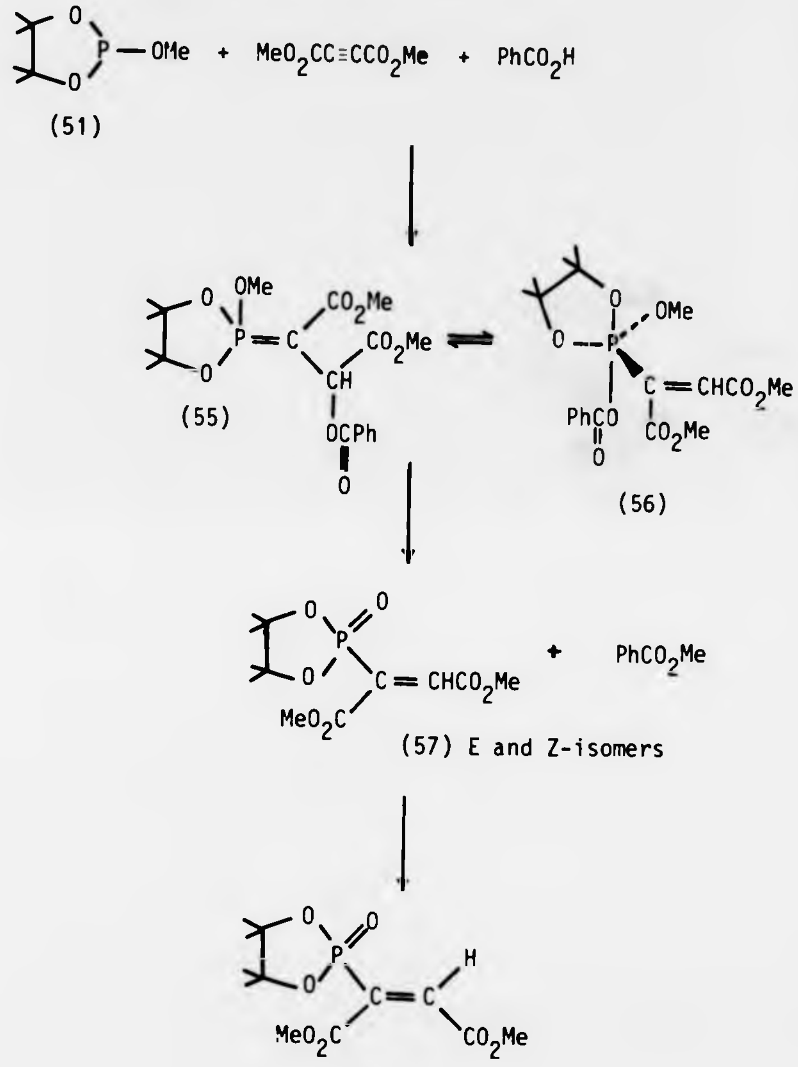
(52)

Interestingly, when the methanol was replaced by phenol in this reaction a quantitative yield of the ylide (53) was initially obtained, although this subsequently underwent thermal rearrangement to give the phosphorane (54).[32,33,37]



(53) (54)

When benzoic acid was used as the protic reagent an equilibrium was observed between the ylide (55) and the phosphorane (56) which appeared to be solvent and temperature dependent (Fig. 13).[32,34,36] The phosphonate (57) was isolated from the reaction mixture as its E-isomer.

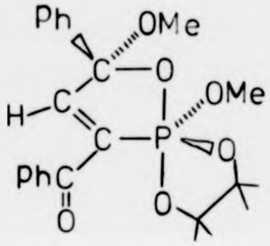


E-isomer

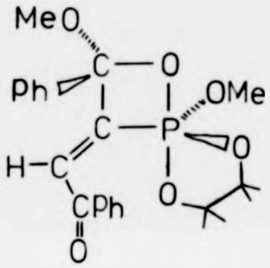
(57)

Fig. 13

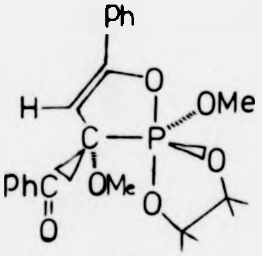
When the reaction of the cyclic phosphite (51) with dibenzoylacetylene in the presence of methanol was investigated at -20 °C, the product was a mixture of the two spirophosphorane isomers (58) and (59).[36,37] The alternative structure (60) was ruled out on the basis of ^1H n.m.r. data.



(58)

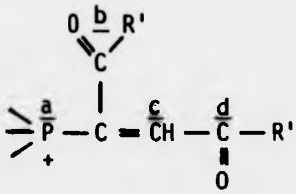


(59)



(60)

In summary therefore, the product of reaction thus depends on the site of attack by the alcohol in the vinylphosphonium intermediate (61).



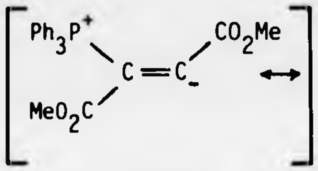
$$\geq\overset{a}{\underset{+}{P}}-\overset{\overset{O\overset{b}{=}C-R'}{|}}{C}=\overset{c}{C}H-\overset{d}{\underset{\overset{\|}{O}}{C}}-R'$$

(61)

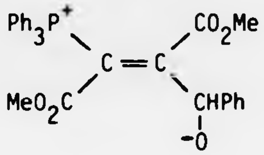
Attack at position a gives a five-coordinate phosphorane such as (52), attack at position c gives an ylide such as (49), and attack at either positions b or d gives a spirophosphorane such as (58) and (59).

(vi) Aldehydes.

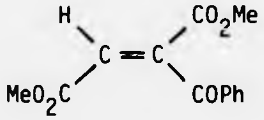
The 1:1 intermediate (29) has also been trapped by benzaldehyde.[38] In this reaction the lactone (63) and alkene (64) were produced. Both can be rationalised as proceeding via the intermediate (65).



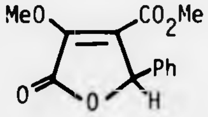
(29)



(65)



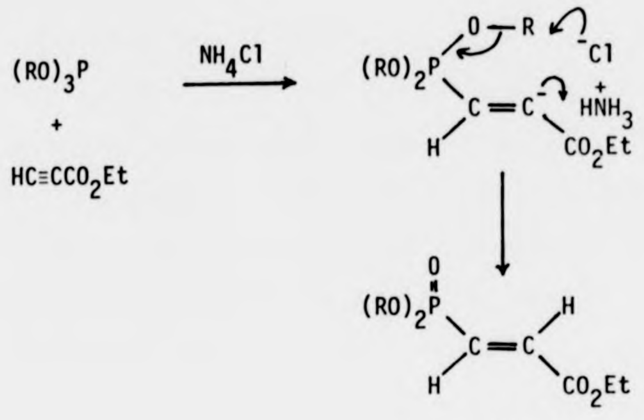
(64)



(63)

(vii) Ammonium Chloride.

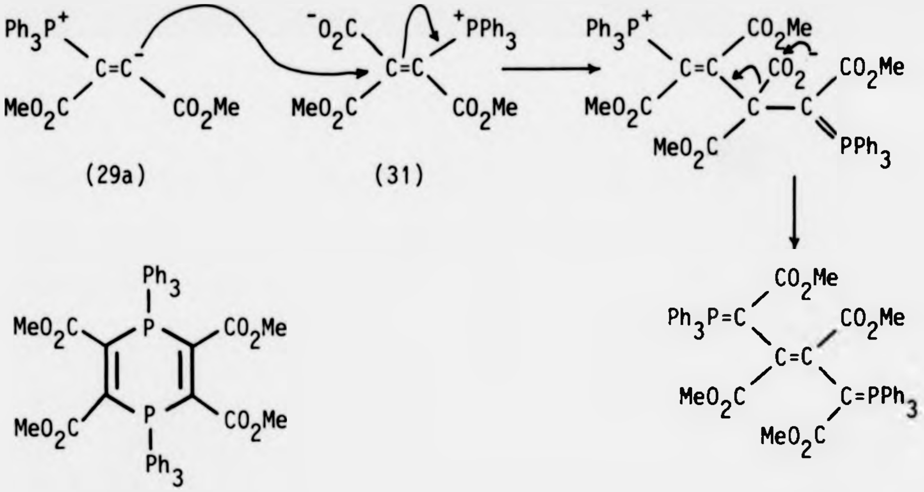
The 1:1 intermediate prepared from the reaction of the trialkyl phosphites with ethyl propiolate, is dealkylated at the phosphonium centre in the presence of ammonium chloride giving a vinylphosphonate (66).[39] (c.f. Fig. 8)


(RO)$_3$P
+
HC≡CCO$_2$Et
NH$_4$Cl
(RO)$_2$P
O
R
$^-$Cl
C
C$^-$
H$\overset{+}{N}$H$_3$
H
CO$_2$Et
O
(RO)$_2$P
C
C
H
H
CO$_2$Et

(66)

3. "2:2 ADDUCTS."

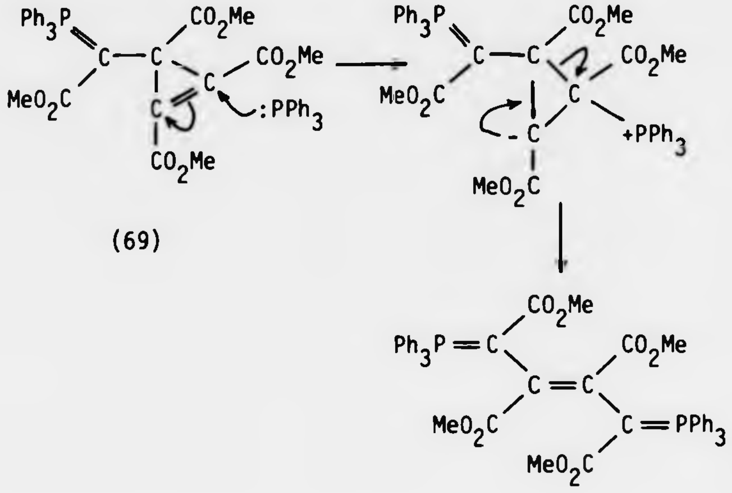
Loss of carbon dioxide from the betaine (31), formed from the reaction of triphenylphosphine with dimethyl acetylenedicarboxylate in the presence of carbon dioxide, occurred rapidly at 50 °C to give a stable orange product. This was initially tentatively assigned the structure of the 1,4-diphosphacyclohexadiene (67),[2] but was later shown to be an alkylidene-1,4-diphosphorane (68).[21] The formation of this 2:2 adduct (68) is believed to involve the reaction of the 1:1 intermediate (29) with the betaine (31), followed by loss of carbon dioxide.



(29a) (31)

(67) (68)

The 1,4-diphosphorane (68) has also been reported to be formed in good yield[40] by the reaction of the unstable adduct (69) with triphenylphosphine. The unstable adduct (69) cyclopropenylmethylidenephosphorane, has been reported to be formed when triphenylphosphine reacts with dimethyl acetylenedicarboxylate at -50 °C.



(69)

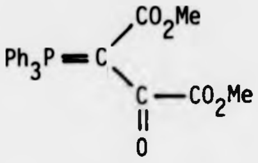
(68)

Ketari and Foucaud[41] report that the stable triphenylphosphine/ copper chloride complex (70) retains the nucleophilic character of the phosphine while modifying its reaction with dimethyl

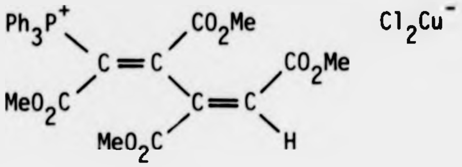
$$(Ph_3P - Cu - Cl)_4$$

(70)

acetylenedicarboxylate. Thus, in the reaction of (70) (1 equiv.) with dimethyl acetylenedicarboxylate (2 equiv.) in benzene the 1,4-diphosphorane (68) was produced in 48% yield. Two by-products, the phosphorane (71) (49%) and the phosphonium salt (72) (3%), were also formed in the reaction.

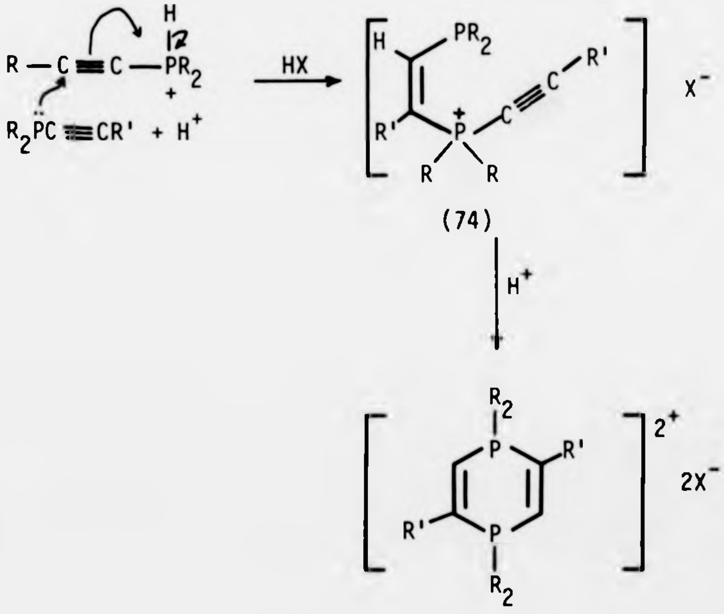


(71)



(72)

When the reaction was carried out in dichloromethane the yield of (68) was reduced to 10% while that of (71) was increased to 70%. Salts of 1,4-diphosphacyclohexadiene (73)[42] are formed from dialkyl- and diaryl-1-alkynylphosphines under acidic conditions via an acid catalysed attack of the phosphine moiety of one molecule on the acetylenic bond of another molecule. Cyclisation of the initially formed intermediate (74) occurs by intramolecular nucleophilic attack on the resulting activated acetylene.

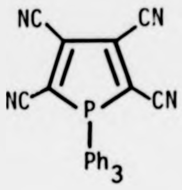


(74)

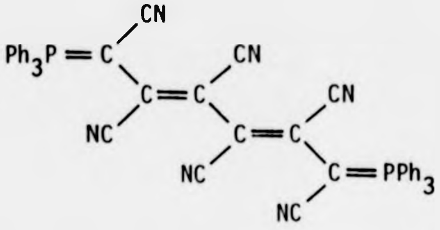
(73)

4. "2:3 ADDUCTS."

Reddy and Weis[43] reported that the reaction between triphenylphosphine and dicyanoacetylene yielded an orange crystalline solid to which they tentatively assigned the structure (75), a five-coordinate (n^5) phosphole.



(75)



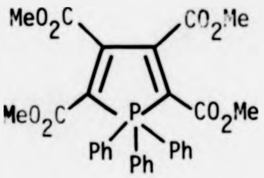
(76)

However, Tebby's group[44,45] have since shown that this adduct is not a phosphole but the 1,6-diphosphorane (76).

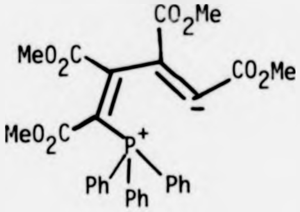
5. "1:2 ADDUCTS."

5.1 Phosphines.

The reaction of triphenylphosphine with dimethyl acetylenedicarboxylate at low temperatures has been investigated by both Johnson and Tebby,[2] and Hendrickson.[46] At -50 °C both groups observed the formation of an unstable intermediate which they identified as a 1:2 adduct. However, while Hendrickson proposed the structure of the η^5-phosphole (77), Johnson and Tebby preferred the zwitterionic structure (78), similar to that proposed by Horner and Hoffmann[17] for the adduct obtained from the reaction of triethylphosphine and dimethyl acetylenedicarboxylate.

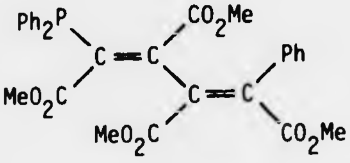


(77)

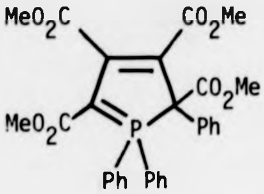


(78)

The charged structure (78) was preferred to the covalent structure (77) by Johnson and Tebby[2] since it was felt to provide more of a driving force for the phenyl migration which was observed on warming this adduct. The rearrangement of the η^5-phosphole (77) was originally thought to give the phosphine (79)[2,46] but this was later corrected on the basis of n.m.r. and other studies which showed the material to be the cyclic ylide (80).[47]

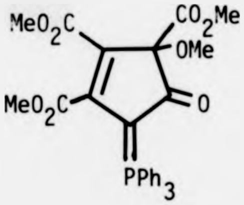


(79)



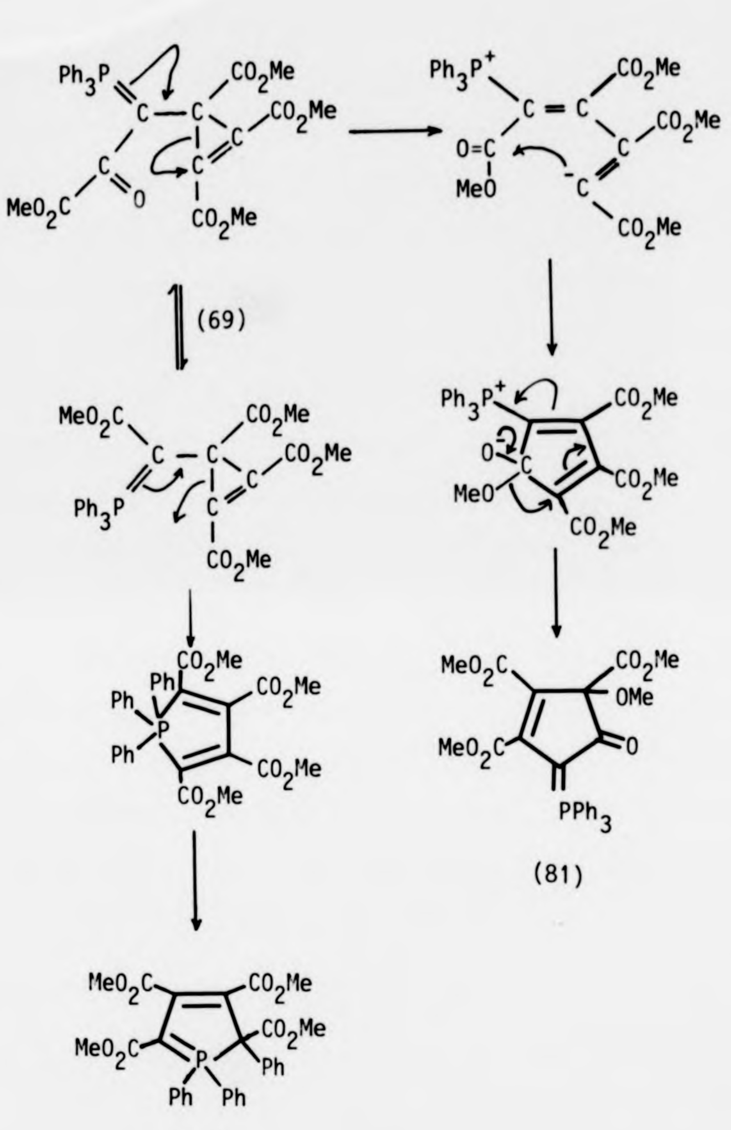
(80)

The cyclic ylide (80) was also formed in reasonable yield (31%) when triphenylphosphine was added to dimethyl acetylenedicarboxylate in ether at room temperature and the mixture then heated under reflux for 1h.[2] However, under these conditions an additional 1:2 adduct was also formed which was identified as the cyclopentenylidenephosphorane (81).[48] Its structure was confirmed by chemical and spectroscopic evidence and by comparison with the corresponding tri-p-toluoylphosphine derivative where the structure was determined by X-ray crystallography.[49]



(81)

Both the cyclic ylide (80) and the cyclopentenylidenephosphorane (81) can be regarded as arising from a common precursor, namely the cyclopropenylmethylidenephosphorane (69) (Fig. 14).



(69)

(80)

(81)

Fig. 14

It is now known that a range of cyclic ylides analogous to (80) can be prepared.[40] Interestingly, when tri-p-toluoyl-, diphenyl-β-chloro, diphenylanisyl-, and diphenyl-p-toluoylphosphines were used the ease of rearrangement from the triaryl n^5-phosphole to the cyclic ylide was found to depend on the nature of the migrating group. The ease of aryl migration was found to be p-chlorophenyl>phenyl>p-toluoyl>anisyl indicating that the ease of migration was favoured by those groups best able to stabilise a negative charge. This is consistent with the order expected for migration from the apical position of a trigorial pyramidally substituted phosphorus atom.[1]

It was confirmed that the aryl migration was intramolecular by reacting a mixture of triphenylphosphine and tri-p-tolylphosphine with dimethyl acetylenedicarboxylate.[40] No mixed substitution was observed in the resulting cyclic ylides. When diphenylvinylphosphine was added to an excess of dimethyl acetylenedicarboxylate the initially formed cycloaddition product (39a) led to the formation of a bicyclic adduct, the phosphabicycloheptadiene (82), which was isolated as the hydrolysis product (83),[11] (Fig. 15).

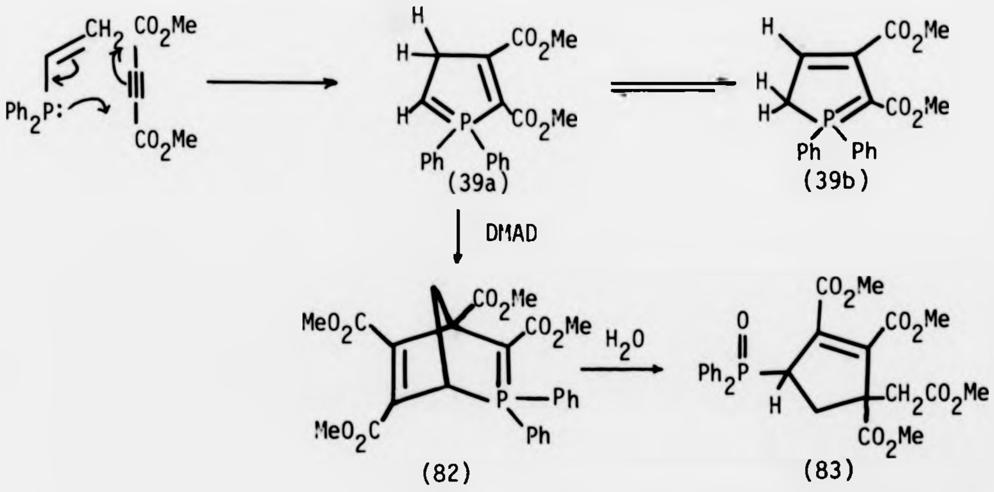
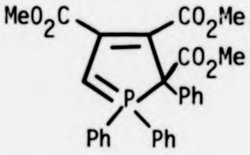


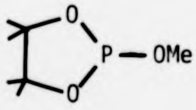
Fig. 15

5.2 Trialkyl phosphites.

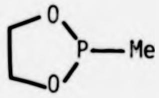
Tebby and Griffiths[50] have reported preliminary studies into the reaction of trimethyl phosphite with dimethyl acetylenedicarboxylate. By using low temperature n.m.r. techniques they were able to monitor the course of the reaction and identify a number of 1:2 intermediates analogous to those proposed in the triphenylphosphine/dimethyl acetylenedicarboxylate reaction for the formation of (80). A more detailed investigation of this reaction forms part of this dissertation and is discussed later. Burgada[35,51] has studied the reaction of the cyclic phosphites (51) with dimethyl acetylenedicarboxylate, [see later discussion].



(80)



(51a)



(51b)

Nuclear Magnetic Resonance (N.M.R.) Spectroscopy.

Since n.m.r. spectroscopy has been used extensively in the work described in this thesis, both to follow reaction pathways and to identify products and intermediates, it is useful to consider at this point those aspects of this subject which have been of importance in our research.

1. CHEMICAL SHIFTS

When nuclei which have an associated magnetic moment (i.e. those for which the spin-quantum number (I) is non-zero) are placed in a magnetic field they are able to absorb radiation in the radio-frequency region of the electromagnetic spectrum. The frequency at which the nuclei resonate is given by the expression:

$$\nu = \frac{\gamma B}{2\pi}$$

Where ν = the resonant frequency

B = the applied magnetic field

γ = the magnetogyric ratio of the nucleus under investigation.

If, however, all the nuclei of a given isotope were to resonate under identical conditions, the amount of information available from the n.m.r. experiment would be severely limited. The usefulness of n.m.r. spectroscopy arises from the fact that nuclei in different chemical environments experience slightly different magnetic fields. This is due to the electrons within the molecule which generate their own local magnetic fields in response to and in opposition to the applied magnetic field. For this reason nuclei in dissimilar chemical environments have slightly different resonant frequencies.

Since in practice it is difficult to measure accurately the high magnetic fields used in n.m.r. spectrometers, it is usual to measure the resonance conditions for a given nucleus relative to an agreed standard. The difference in resonance conditions is termed the chemical shift (δ) which is given by the expression:

$$\delta = \frac{\nu_{\text{sample}} - \nu_{\text{reference}}}{\nu_{\text{reference}}} \times 10^6$$

The δ scale is dimensionless, but since a factor of 10^6 is included to give δ acceptable values it is quoted in units of p.p.m. Chemical shift values determined on all n.m.r. spectrometers are directly comparable, regardless of their magnetic field strengths.

2. ELECTRON-COUPLED NUCLEAR SPIN-SPIN COUPLINGS

Although one might expect the nuclei in a particular chemical environment to resonate at a well defined frequency one often observes that such nuclei give rise to a series of resonance lines. This is due to the fact that the magnetic field experienced by the resonating nuclei is influenced by the presence of other magnetic nuclei in the molecule. This interaction is known as electron-coupled nuclear spin-spin interaction since the information about other magnetic nuclei in the molecule is transmitted via the bonding electrons between the coupled nuclei. This coupling information can be transmitted over several bonds, but diminishes rapidly as the number of bonds increases. It is therefore not usual to observe couplings when the interacting magnetic nuclei are separated by more than four or five bonds.

The number of resonance lines observed in the signal from a nucleus in a given chemical environment will therefore depend on the number of magnetic nuclei it is interacting with and the magnitude of these interactions.

In the simplest case, the "first-order" situation,[52] the number of lines observed for a particular resonance will be given by the expression (2nI + 1), where n is the number of equally coupled nuclei, and I is the spin-quantum number of the nuclei. The relative intensities of these lines will be given by the coefficients of the binomial expression $(a + 1)^n$, where n is the number of observed lines. If the spectrum cannot be interpreted on this basis then the spectrum is likely to be "second-order",[52] and in these circumstances it is usually necessary to use a computer to interpret the coupling information. Fortunately, in much of the ^{13}C and ^{31}P n.m.r. work carried out during our studies it was possible to interpret the spectra by assuming that they approximated to the "first-order" situation.

It is also important to note that the coupling information from a given nucleus can be suppressed by irradiating that nucleus at its resonance frequency. In this way it is possible to remove the coupling information from a resonating nucleus so that it is observed as a single resonance line.

3. ^{31}P NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

3.1 ^{31}P N.m.r. Spectroscopy

Phosphorus is monoisotopic (100% natural abundance ^{31}P), and having a non-zero spin quantum-number ($I = \frac{1}{2}$) it is a magnetically active nucleus. As a consequence, it is possible to study the ^{31}P nucleus directly by n.m.r., or to observe its influence on the spectra of other magnetically active nuclei in the molecule, such as, ^{1}H and ^{13}C.

From its inception ^{31}P n.m.r. spectroscopy has proved to be an invaluable asset to the organophosphorus chemist and during the course of our investigations we have relied heavily on this technique to monitor the course of reactions and to provide a quick and convenient means of identifying the general nature of the products being formed.

Fortunately, organophosphorus compounds frequently contain only a small number of phosphorus atoms and in many cases there is only one phosphorus atom present in the molecule. Thus, unlike the situation in ^{1}H and ^{13}C n.m.r. spectroscopy where each compound gives rise to a reasonably complex spectrum, in ^{31}P n.m.r. spectroscopy we frequently only observe a single signal from a given compound. If the couplings to the protons in the molecule are removed from this signal, by irradiation of the proton nuclei, this signal can be simplified to give a single sharp absorption. It is therefore possible to identify the ^{31}P n.m.r. signal from a given component even in the spectrum of quite a complex mixture.

3.2 ^{31}P N.m.r. Chemical Shifts

The range of chemical shifts observed in ^{31}P n.m.r. spectroscopy[53,54] is considerably larger than that observed in ^{1}H and ^{13}C n.m.r. spectroscopy. This is to some extent a consequence of the ability of the phosphorus atom to adopt a range of co-ordination numbers (three to four is common while two and six co-ordination are rather rare). The co-ordination determines the overall shape and bond angles at the phosphorus. The electrons in the 3p (and occasionally 3d) orbitals make a direct contribution to the shielding of the ^{31}P nucleus, while the type and number of substituents adjacent to the phosphorus also contribute to the shielding.

The largest reported ^{31}P n.m.r. chemical shift appeared to be that of the diphosphorane (84)[55] which has a value of δ_P 598.6 p.p.m.

$$[(H_3C)_3Si]_3C-P=P-C[Si(CH_3)_3]$$

(84)

In accordance with the I.U.P.A.C. convention,[56] ^{31}P n.m.r. chemical shifts are reported in this thesis with reference to 85% H_3PO_4, with positive shifts to low field of the reference.

3.2.1 Tri-co-ordinate compounds

There have been many studies concerned with the ^{31}P n.m.r. spectroscopy of trivalent organophosphorus compounds, such as phosphines.[53,57] It is evident from the collated data that the chemical shifts of tertiary phosphorus compounds are very sensitive to the nature of the substituents since their ^{31}P n.m.r. chemical shifts cover a wide range.

Aspects of the ^{31}P n.m.r. chemical shifts of tertiary organophosphorus compounds, including an assessment of the effects of substituents, have been considered in some detail elsewhere.[57b]

3.2.2 Tetra-co-ordinate compounds

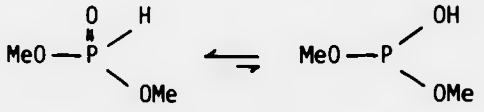
Tetra-co-ordinate organophosphorus compounds containing the phosphoryl grouping (P = O) and with alkyl or aryl substituents generally resonate within the range $\delta(^{31}P)$ 15 to 50 p.p.m., whereas the corresponding phosphonium salts and phosphorus ylides usually resonate about δ_P 20 to 45 p.p.m.[58]. However, in cases where there are a number of oxygen atoms attached to the phosphorus i.e. alkoxy groups, lower field chemical shifts are reported due to deshielding, a number of such compounds are found in this thesis.

3.2.3 Penta-co-ordinate compounds

Penta-co-ordinate organophosphorus compounds are usually more highly shielded than the tri- and tetra- co-ordinated compounds and resonate at relatively high field $\delta(^{31}P)$ -30 to -100 p.p.m.[58] Those five co-ordinated phosphorus compounds in which the phosphorus is covalently bonded to five carbon atoms[59] show the greatest shielding of the phosphorus atom and tend to resonate in the region $\delta(^{31}P)$ -85 to -100 p.p.m.

3.3 Proton-Phosphorus coupling (J_{PH})

Although it is usual to decouple the proton couplings to the phosphorus atom when measuring chemical shifts, the reintroduction of the proton-coupling can be very informative in some circumstances. Couplings to directly bonded protons is immediately apparent in view of the large value of $^1J_{PH}$ observed (1000 Hz).[60] It was thus possible, for example, to show that dimethyl phosphite exists as the four co-ordinate isomeric form (85) rather than its trivalent form (86).



(85) (86)

Couplings to more distant protons are less strong so that, for example, the value of the coupling to the methoxy protons in (85) [$^3J_{PH}$] was only 12 Hz.[61] However, it can be seen that the doublet of septet pattern observed for (85) in the proton-coupled ^{31}P n.m.r.

spectrum is highly informative since it indicates the presence not only of the directly bonded proton, but also the two methoxy groups adjacent to the phosphorus.

4. ^{13}C NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

4.1 ^{13}C N.m.r. Spectroscopy

Although the ^{12}C nucleus is non-magnetic, the ^{13}C nucleus, like the ^{31}P and ^{1}H nuclei has a spin-quantum number (I) of ½ and can thus be studied by n.m.r. Fortunately, since the natural abundance of the ^{13}C nucleus is only about 1%, the likelihood of two adjacent ^{13}C nuclei normally being present in the molecule is exceedingly small so that couplings between the ^{13}C nuclei will not be observed. Since the couplings to the protons in the molecule can be removed instrumentally (see later section) it is therefore usually possible to produce a ^{13}C n.m.r. spectrum in which the carbons in a given chemical environment resonate as a single sharp line.

In the case of organophosphorus compounds however, couplings between the ^{31}P and ^{13}C nuclei can occur. In the ^{13}C n.m.r. spectrum of a molecule containing a single phosphorus atom, the presence of the phosphorus atom will result in the splitting of certain resonance signals into doublets. Since the size of the J_{PC} coupling tends to decrease with increasing separation between the coupled nuclei the observed J_{PC} coupling on a given carbon signal can be used to assess the proximity of this carbon to the phosphorus. In addition, the size of the $^{1}J_{PC}$ coupling depends on the nature of the bonding between the two coupled nuclei. It is therefore usually possible to distinguish between, for example, a phosphonate and a phosphonium ylide on the basis of the value of the phosphorus coupling to the α-carbon.

As with ^{1}H and ^{31}P n.m.r. spectroscopy the chemical shift of a given carbon site within a molecule will depend on its chemical environment and this information can clearly be of value for structure elucidation. Moreover, the reintroduction of the proton--couplings into the ^{13}C n.m.r. spectrum quickly enables the protonation state of the individual carbons in the molecule to be determined. The application of chemical shift and coupling data in ^{13}C n.m.r. spectroscopy has been covered in a number of texts.[52,62]

Since ^{13}C labelling experiments are described later in this thesis it is of interest to consider the effect on the ^{13}C n.m.r. spectrum of introducing a high degree of ^{13}C isotopic enrichment at one site within a molecule.

The most obvious effect in the ^{13}C n.m.r. spectrum of the ^{13}C labelling of a particular carbon site within a molecule is that the intensity of the n.m.r. signal for that site is dramatically increased. The increase is often in the order of ninety times, depending on the isotopic purity of the precursor used to prepare the labelled compound.

At these high levels of isotopic enrichment, however, a second effect occurs. In these circumstances the likelihood of finding two ^{13}C nuclei in the same molecule is much increased, so that, coupling between ^{13}C nuclei can no longer be ignored. The ^{13}C n.m.r. signals of carbons adjacent to the site of isotopic enrichment will therefore be observed as doublets. This in turn can be used as an aid to assignment.

4.2 The effects of deuteration on ^{13}C n.m.r. spectra

Deuterium labelling experiments have also been used in this work as an unambiguous method of assigning resonance in the ^{13}C n.m.r.

spectra of certain organophosphorus compounds, or for investigating the mechanism of a reaction [see Discussion section].

The replacement of a proton on a carbon atom by a deuterium atom results in a marked diminution of the ^{13}C n.m.r. signal of the deuterated carbon, in the noise-decoupled spectrum. There are several reasons for this. As deuterium (D) has a spin-quantum number (I) of 1 it will split the ^{13}C n.m.r. signal into three lines as predicted by the expression (2nI + 1) [see earlier section]. Moreover, since these lines are found to be of equal intensity the signal intensity will have been reduced by a factor of three as a result of this coupling. Interestingly, since the magnetic moment of the deuterium atom is only about one seventh of that of the proton, the size of the couplings are reduced proportionally and J_{CD} is found to equal 0.15 J_{CH}.

There are however two further effects which also reduce the signal intensity of the deuterated carbon atom. Firstly, the nuclear Overhauser effect is lost since in the proton noise-decoupled ^{13}C n.m.r. spectrum no irradiation of the deuterium atoms occurs. Secondly, the relaxation times (T_1) of a deuterated carbon atom can be considerably longer than that of the protonated carbon which, under normal operating conditions, will again lead to a reduction in signal intensity. This longer relaxation time is due to the reduced effectiveness of the deuterium over the hydrogen atom in the dipole--dipole relaxation mechanism. It is interesting to note that in addition to the deuterated carbon resonance a separate ^{13}C n.m.r. resonance signal may also be seen for any residual protonated carbon. An isotope effect occurs which usually results in a slight upfield shift of the ^{13}C-D signal relative to the ^{13}C-H signal (about 0.2 p.p.m. per deuterium atom). This effect may also be experienced by carbon atoms adjacent to the site of deuteration.

5. FOURIER-TRANSFORM NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

5.1 Fourier-Transform N.m.r. Spectroscopy

Although n.m.r. spectroscopy has proved to be an invaluable technique for many years, it is only since the advent of Fourier transform n.m.r. spectrometers, with their sophisticated decoupling facilities, in the early 1970's that it has been possible to study on a routine basis the spectra of insensitive nuclei, such as ^{13}C, or dilute solutions.

Early Continuous-Wave spectrometers were designed primarily for studying the ^{1}H nucleus and were relatively insensitive. The sensitivity of such spectrometers could, however, be increased by repeatedly scanning the region of the spectrum of interest and accumulating the data in a computer. At points in the spectrum where no signal was present the signal intensity was largely due to random electronic "noise" and thus gradually averaged to zero. On the other hand, where a small signal was present in the spectrum this was reinforced by subsequent scans until a satisfactory signal intensity had been obtained. The quality of the resulting spectrum was then expressed as a signal to noise ratio. Since the increase in signal to noise ratio is directly proportional to the square root of the number of scans, increases in the signal to noise ratio by signal accumulation became progressively more difficult to achieve.

It is evident that to achieve a reasonable improvement in the signal to noise ratio that it would be necessary to accumulate hundreds, if not thousands of scans. Since a single scan could take several minutes accumulation times were impractically long for routine work.

The weakness of the continuous-wave n.m.r. spectrometer lay in the fact that at any one instant in time information was only being obtained about one particular frequency. This limitation was overcome in the Fourier transform n.m.r. spectrometer which was designed to obtain information about all frequencies in the spectra simultaneously. To do this the sample was placed in a strong homogenous magnetic field and then subjected to a short pulse of radio-frequency radiation at the frequency appropriate for the excitation of the nucleus being studied. Switching the transmitter power on and off to produce the pulse, generated a broad envelope of frequencies around the main transmitter frequency ensuring that all nuclei of a given type in the molecule were irradiated at their resonant frequencies.

Since energy was absorbed during the pulse, the system needed to subsequently lose energy to return to its equilibrium state. As the excited nuclei relax they emit energy at their resonant frequencies and this emission of energy (the free induction decay) is detected by the spectrometer. This data is then analysed by a computer to obtain information about the frequency components within the energy emitted, and hence the resonance frequencies of the nuclei in the sample.

Since the acquisition of the free induction decay can often take less than a second it can be seen that the sample can be repeatedly pulsed and the decays stored much more quickly than with the Continuous Wave n.m.r. spectrometer. The accumulated free induction decay is processed at the end of data acquisition to obtain the conventional frequency spectrum.

5.2 Heteronuclear decoupling techniques

Modern Fourier Transform n.m.r. spectrometers are equipped with a range of heteronuclear decoupling facilities.

5.2.1 Proton noise-decoupling

By applying a broad band of decoupling power across the whole of the proton region of the spectrum it is possible to remove the couplings from these protons. This not only simplifies the spectra of the ^{31}P and ^{13}C nuclei in the molecule, by collapsing multiplets into singlets but as a result it also increases the signal to noise ratio of the signals. This effect is further enhanced by the nuclear Overhauser effect which, in the case of ^{13}C n.m.r. and proton noise-decoupling, can result in an increase in the signal to noise ratio by as much as a factor of 3. The net effect of proton noise-decoupling is thus a large reduction in the time required to obtain this type of spectrum as compared with the proton-coupled spectrum.

5.2.2 Off-resonance proton decoupling

This technique which we will discuss in the context of ^{13}C n.m.r. enables the number of protons directly bonded to each carbon atom to be determined without the severe loss in signal to noise ratio which would result if the proton-decoupler were to be switched off.

In essence, a low decoupler power is applied to the proton region of the spectrum, usually centred at one extreme end of the normal range of proton shifts. This decoupler power removes the smaller longer-range J_{CH} couplings and reduces the splitting arising from the directly bonded protons. Although the remaining splittings are no longer true coupling constants the multiplicities of the signals are maintained. In off-resonance spectra methyl carbon atoms would be observed as quartets, methylene carbons as triplets, methine carbons as doublets, and quarternary carbons as singlets.

5.2.3 Gated decoupling techniques

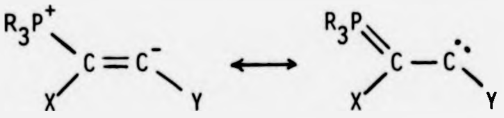
The irradiation of the protons in a molecule has two effects on the ^{13}C n.m.r. spectrum of that molecule. Firstly, it leads to the removal of the proton coupling from the ^{13}C n.m.r. signals and secondly, it increases the intensity of certain signals due to the nuclear Overhauser effect (n.O.e.).[63] Fortunately while the Overhauser effect is an equilibrium effect and takes time to build up, the effects of decoupling are instantaneous. For this reason it is possible by switching the decoupler on and off at particular times during the cycle (i.e. by "gating" the decoupler) to obtain one or other of these two effects without the other.

In this thesis we have frequently needed to obtain the proton-coupled ^{13}C n.m.r. spectrum of a molecule and in these circumstances it has been desirable to make use of any effects which would improve the signal to noise ratio in the spectrum. By switching the decoupler off only during the data acquisition period of the cycle, it is possible to build up and then maintain the enhancement arising from the nuclear Overhauser effect while, at the same time obtaining a spectrum in which the proton couplings are present. The reverse situation is also possible and this is useful when the true intensities of the lines in the ^{13}C n.m.r. spectrum are of interest.

CHAPTER 1

An Investigation of the Reaction of Trivalent Phosphorus Compounds with Electrophilic Acetylenes.

Acetylenes, such as dimethyl acetylenedicarboxylate, which have two electron-withdrawing substituents are electrophilic and are susceptible to attack by a range of nucleophiles [10,67,68] including trivalent organophosphorus compounds [see Introduction]. The nature of the 1:1 intermediate initially formed on the reaction of a trivalent phosphorus compound with an electrophilic acetylene is of particular interest since one can envisage both anionic (1b) and carbenoid (1a) forms which contribute to the overall structure.



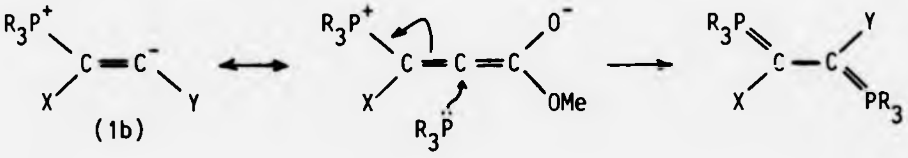
(1b) (1a)

The relative importance of these two canonical forms would be expected to depend not only on the nature of the groups X and Y on the acetylene but also on the substituents on the phosphorus atom. It was therefore of interest to compare the reactivity of the 1:1 intermediates (1; R = Ph, X = Y = CO_2Me) formed from the reaction of dimethyl acetylenedicarboxylate with triphenylphosphine with those prepared from other trivalent phosphorus compounds or other electrophilic acetylenes.

1. THE REACTION OF DIMETHYL ACETYLENEDICARBOXYLATE WITH AN EXCESS OF SOME TERTIARY PHOSPHORUS COMPOUNDS.

1.1 The reaction of dimethyl acetylenedicarboxylate with excess trialkyl phosphite

The reaction of dimethyl acetylenedicarboxylate with excess triarylphosphine has been studied in some detail [see Introduction]. It is generally accepted that the formation of the 1,2-diphosphorane in this reaction proceeds via the reaction of the initially formed 1:1 intermediate with further phosphine. Early work viewed this as a nucleophilic attack by the phosphine on the 1:1 intermediate (Fig. 16) but, since carbene insertion into a phosphine also leads to ylide formation[69] the reaction of the 1:1 intermediate in its carbenoid form with the phosphine cannot be excluded.

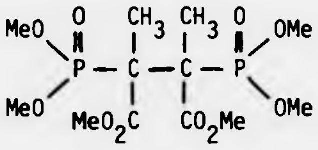


(1b)

X,Y = CO_2Me

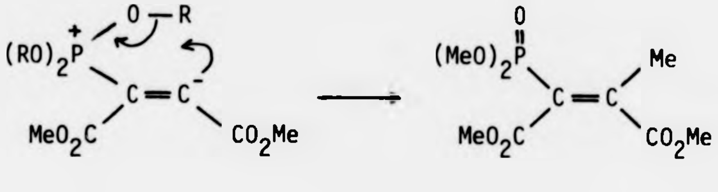
Fig. 16

In contrast, Griffin and Mitchell have reported the formation of the diphosphonate (14) from the reaction of dimethyl acetylenedicarboxylate with two molar equivalents of trimethyl phosphite.[12]

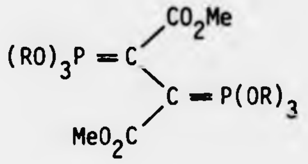


(14)

Griffin and Mitchell[12] have explained these observations by proposing that the initial product is a vinylphosphonate (15) which is produced by rearrangement of the initially formed 1:1 intermediate (87; R = Me).


(87; R = Me)　(15)

Reaction of the vinylphosphonate (15) with trimethyl phosphite followed by rearrangement then leads to the observed diphosphonate (14). We have therefore investigated the reaction of dimethyl acetylenedicarboxylate with excess trimethyl phosphite using ^{31}P n.m.r. techniques to monitor the course of the reaction to see if such a reaction route does occur. However, despite using a range of reaction conditions we were unable to find any evidence for the large scale formation of the proposed vinylphosphonate (15) or the diphosphonate (14). We found that the products from the reaction of trimethyl and triethyl phosphite with dimethyl acetylenedicarboxylate were highly dependent on the ratio of the reactants, the solvent and temperature used for the reaction, and the rate at which the reactants were mixed together. Even when the phosphite was kept in excess the reaction products were often shown by ^{31}P n.m.r. to be complex mixtures. Although these mixtures included signals which were later assigned to the expected 1,2-diphosphorane (88; R = Me, Et), many of the smaller phosphorus signals observed still remain to be identified.



(88)

After a number of experiments, conditions were found where the formation of the 1,2-diphosphoranes (88; R = Me, Et) could be carried out in sufficiently high yield (about 40% as indicated by ^{31}P n.m.r. spectroscopy) to enable attempts to be made to isolate them from their reaction mixtures. However, attempts to purify the 1,2-diphosphoranes (88; R = Me, Et) by chromatographic techniques or by distillation results in their decomposition. Further efforts were therefore made to find conditions which would minimise the formation of unwanted by-products and which, at the same time, would be readily reproducible. Fortunately, by slow addition of a dilute solution of dimethyl acetylenedicarboxylate to a two molar equivalent of the trialkyl phosphite, cooled in an ice bath, it was possible to prepare clean samples of both the methoxy and ethoxy substituted diphosphoranes (88; R = Me) and (88; R = Et). Attempts to remove small quantities of impurities from the ethoxy substituted system (88; R = Et) by trituration using diethyl ether were, however, only partially successful. Although the final product, a viscous oil, was pure by ^{31}P n.m.r. spectroscopy it did not give a satisfactory combustion analysis.

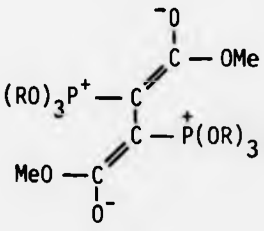
When the preparation of the methoxy substituted diphosphorane (88; R = Me) was carried out, however, a yellow precipitate gradually settled from the reaction mixture. This was shown by ^{31}P n.m.r.

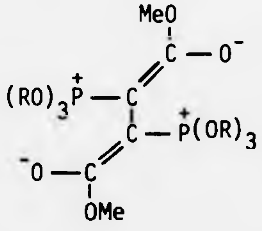
spectroscopy to have a spectrum consistent with that expected for the required 1,2-diphosphorane (88; R = Me). This product also gave a combustion analysis consistent with the 1,2-diphosphorane (88; R = Me) and the mass spectrum showed the expected molecular ion.

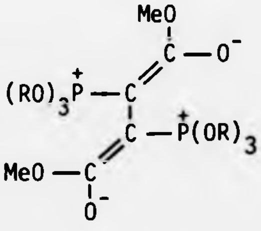
Despite earlier indications to the contrary it had therefore been possible to develop conditions which enabled the 1,2-diphosphorane (88; R = Me) to be produced in a pure form in essentially quantitative yield.

1.1.1 ^{31}P N.m.r. spectrum of the 1,2-diphosphorane (88; R = Me).

The ^{31}P n.mr. spectrum of the 1,2-diphosphorane (88; R = Me) in deuterochloroform at room temperature showed six sharp resonance lines at δ_P 64.16, 62.77, 62.52, 61.42, 61.17, and 60.15 p.p.m. (see Plate 1). The spectrum was, however, temperature dependent so that warming the sample caused broadening and the eventual coalescence of some of these lines. This information was interpreted as indicating that at room temperature the 1,2-diphosphorane (88) exists as three slowly interconverting conformers (88a, 88b, 88c).


(88a)


(88b)

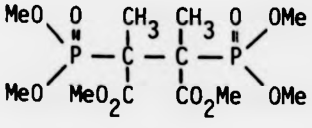

(88c)

This type of behaviour is a characteristic feature of alkylidenephosphoranes containing the α-alkoxycarbonyl group[5] and is due to the restricted rotation about the bond to the α-methoxycarbonyl group arising from the partial double bond character in that bond. A similar effect was observed in the low temperature ^{1}H n.m.r. spectrum of the 1,2-diphosphoranes prepared by the reaction of triphenylphosphine with dimethyl acetylenedicarboxylate.[4]

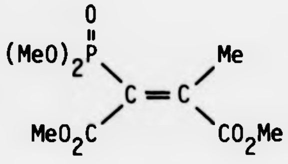
It should be noted that while structure (88a) and (88b) are symmetrical and would thus each be expected to give a single phosphorus resonance, (88c) is asymmetrical. The central four resonance lines in the ^{31}P n.m.r. spectrum of the 1,2-diphosphorane (88; R = Me) (Plate 1) can thus be interpreted as an AB type system ($^{3}J_{PP}$ 10 Hz) resulting from the difference in the ^{31}P n.m.r. shifts of the two phosphorus atoms in (88c). The ^{31}P n.m.r. spectrum of the 1,2-diphosphorane (88; R = Me) is thus more correctly described as having four resonances at δ_P 64.16, 62.64 (d, $^{3}J_{PP}$ 10 Hz), 61.29 (d, $^{3}J_{PP}$ 10 Hz), and 60.15 p.p.m. For the ^{31}P n.m.r. spectral data of the 1,2-diphosphorane (88; R = Et) see Experimental section.

1.1.2 Investigation of the reported preparation of the 1,2-diphosphonate (14) from the reaction of trimethyl phosphite with dimethyl acetylenedicarboxylate.

We next considered the reported formation of the 1,2-diphosphonate (14) by the reaction of trimethyl phosphite with dimethyl acetylenedicarboxylate and the suggestion that this reaction proceeded via the vinyl phosphonate (15).[12]



(14)



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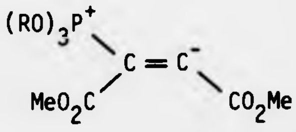


(87)

^{31}P N.m.r. spectrum of 1,2-bismethoxycarbonyl ethane-1,2-bis(trimethoxyphosphorane) (88; R = Me) (proton decoupled).

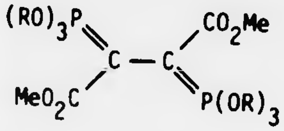
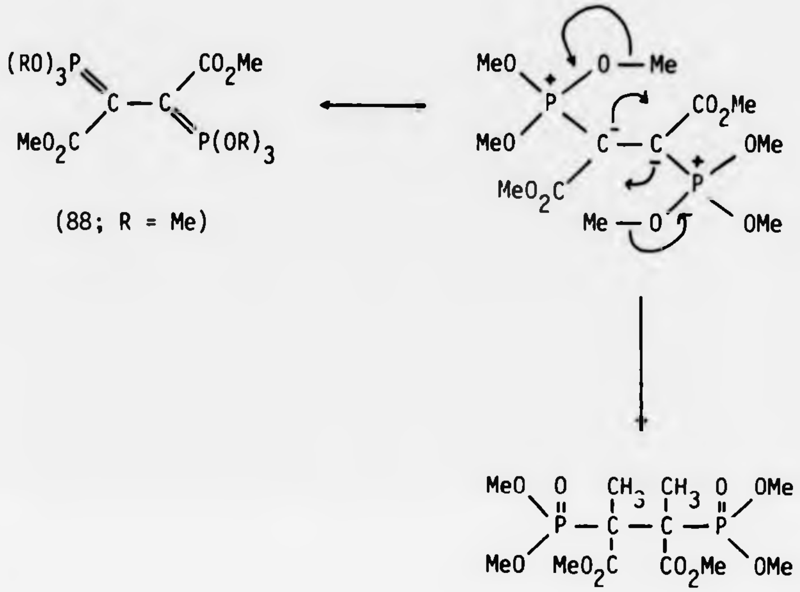


Plate 1

In view of our early observations which clearly indicated the high reactivity of the 1:1 intermediate (87) towards trialkyl phosphite, it seemed unlikely that the proposed formation of the vinyl phosphonate (15) would occur to any significant extent in the presence of excess trimethyl phosphite. We, therefore, felt that the observed formation of the diphosphonate (14) by Griffin and Mitchell[12] might be better explained by proposing that the 1,2-diphosphorane (88; R = Me) was formed initially, but then underwent thermal rearrangement during the purification procedure used by these workers which involved a distillation at about 190 °C (see Fig. 17). To test this theory the work of Griffin and Mitchell[12] was repeated. However, this time the course of the reaction was monitored by ^{31}P n.m.r. spectroscopy.

As expected, the product prior to distillation contained about 80% of the 1,2-diphosphorane (88; R = Me) together with a number of other minor products. However, attempts to rearrange this material to the 1,2-diphosphonate (14) were unsuccessful. When distillation was carried out under the conditions described by Griffin and Mitchell[12], the decomposition of the 1,2-diphosphorane (88; R = Me) occurred and a variety of products were produced. There was, however, no clear evidence for the formation of significant quantities of the 1,2-diphosphonate (14). The distillation of the 1,2-diphosphorane (88; R = Me) was therefore carried out under a variety of conditions to see if the formation of the 1,2-diphosphonate (14) could be achieved. However, although there was some variation in the ratio of the products formed, we were unable to find any spectroscopic evidence for the formation of significant quantities of the 1,2-diphosphonate (14).



(88; R = Me)

(14)

Fig. 17

Attempts to use lower temperatures to effect the rearrangement were also unsuccessful. Thus, when a sample of the 1,2-diphosphorane (88; R = Me) was heated under nitrogen at 150 °C for 7h, there was no apparent change in the ^{31}P n.m.r. spectrum of the product.

We must therefore conclude that if Griffin and Mitchell did observe the formation of substantial quantities of the 1,2-diphosphonate (14) then, either there may have been some component present within their reaction mixture to catalyse the required rearrangement or the formation of the 1,2-diphosphonate (14) occurs within a limited range of conditions which we were unable to reproduce. It is interesting to note that the original distillate did contain a signal in the ^{1}H n.m.r. spectrum characteristic of a methyl group, as might be expected for the 1,2-diphosphonate (14), but this was shown to arise from the presence of some dimethyl methylphosphonate in the sample.

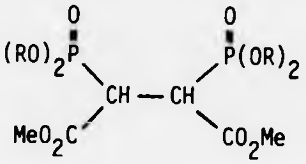
1.1.3 Reactions of the 1,2-diphosphoranes (88; R = Me, Et).

Having prepared the 1,2-diphosphoranes (88) it was of interest to investigate their stability and reactivity.

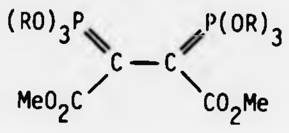
1.1.3.1 Reaction with water.

In order to test the stability of the 1,2-diphosphorane (88; R = Me) towards water an aqueous solution of this material was prepared and its progress monitored by ^{31}P n.m.r. spectroscopy. After standing for 2 days at room temperature the solution of the 1,2-diphosphorane (88; R = Me) showed the formation of three phosphorus components giving ^{31}P n.m.r. signals at δ_P 23.62, 21.88, and 2.4 p.p.m. The component at δ_P 2.4 p.p.m. (30% of the

^{31}P n.m.r. signal intensity) was readily identified by its proton-coupled ^{31}P n.m.r. signal as trimethyl phosphate while, the shifts of the other two signals suggested that they might be phosphonates. After concentrating the aqueous solution crystallisation occurred. These colourless crystals were shown to give rise to ^{31}P n.m.r. signals at δ_P 21.77 and 21.55 p.p.m. and were subsequently shown to be tetramethyl 1,2-dimethoxycarbonylethane-1,2-diphosphonate (17; R = Me).



(17)



(88)

Water had thus led to the protonation and subsequent dealkylation of the 1,2-diphosphorane (88; R = Me).

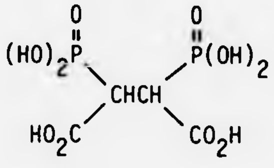
1.1.3.2 Reaction with anhydrous hydrogen bromide

To confirm that the product formed in the reaction of the 1,2-diphosphorane (88; R = Me) with water was the 1,2-diphosphonate (17; R = Me) the former was treated with anhydrous hydrogen bromide in chloroform. This resulted in the orange colour of the solution being discharged and the immediate formation of the desired 1,2-diphosphonate (17; R = Me) which was shown to be identical to the product isolated from the aqueous solution of the 1,2-diphosphorane (88; R = Me). Similarly, treatment with anhydrous hydrogen bromide of a solution of the 1,2-diphosphorane (88; R = Me) in chloroform gave an almost quantitative yield of the 1,2-diphosphonate (17; R = Et). The ^{31}P n.m.r.

chemical shifts of the two diastereoisomers of the 1,2-diphosphonate (17; R = Et) were observed at δ_P 19.4 and 19.1 p.p.m. with relative ratios of 1:7 respectively. Nicholson[14] has also reported the preparation of the 1,2-diphosphonate (17; R = Me), from the reaction of dimethyl phosphite with dimethyl acetylenedicarboxylate.

1.1.3.3 Reaction with concentrated hydrochloric acid.

The treatment of the 1,2-diphosphoranes (88; R = Me, Et) with concentrated hydrochloric acid for a short period at 100 °C or for several days at room temperature led not only to the protonation and dealkylation of the 1,2-diphosphoranes, but also the hydrolysis of the carboxylic and phosphonate esters. This therefore resulted in the formation of the 1,2-dicarboxylic acid (89) which was isolated as a hygroscopic white solid.



(89)

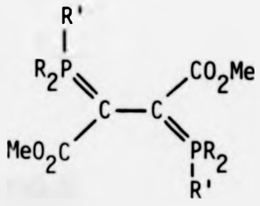
1.1.3.4 Other reactions.

The 1,2-diphosphoranes (88; R = Me, Et) were found to be unreactive towards alkylation by methyl iodide and failed to give a Wittig type reaction when heated under reflux with 4-nitrobenzaldehyde in toluene.

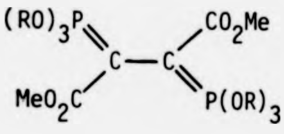
1.2 The reaction of dimethyl acetylenedicarboxylate with excess dialkyl phosphonites.

We have confirmed that the reaction of excess dialkyl phosphonites with dimethyl acetylenedicarboxylate proceeds as expected to give the appropriate 1,2-diphosphoranes (90; R = alkyl or aryl; R' = alkoxy). Thus, the 1,2-diphosphoranes (90; R = OMe, R' = Me), (90; R = OMe, R' = Ph), and (90; R = OEt, R' = Ph) were prepared by the reaction of dimethyl acetylenedicarboxylate with excess dimethyl methylphosphonite, dimethyl phenylphosphonite, and diethyl phenylphosphonite respectively. These 1,2-diphosphoranes showed the characteristic ^{31}P n.m.r. signal pattern which was observed for the 1,2-diphosphorane (88; R = Me) (see Plate 1). The ^{31}P n.m.r. spectral data for the 1,2-diphosphoranes (90; R = OMe, R' = Me), (90; R = OMe, R' = Ph), and (90; R = OEt, R' = Ph) is given in Table 1.

The 1,2-diphosphorane (90; R = Ph, R' = OMe) was also prepared from methyl diphenylphosphonite and once again showed the expected six-line resonance pattern in the ^{31}P n.m.r. spectrum (Table 1).



(90)



(88)

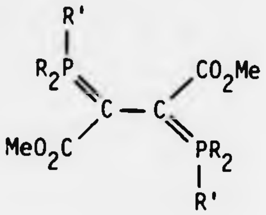
2. THE REACTION OF SOME TERTIARY PHOSPHORUS COMPOUNDS WITH AN EXCESS OF DIMETHYL ACETYLENEDICARBOXYLATE

The reaction of triphenylphosphine with an excess of dimethyl acetylenedicarboxylate has been shown to lead to the production of a number of stable products[40,44,45] by routes which can be rationalised as proceeding via the initially formed 1:1 intermediate

TABLE 1

^{31}P N.m.r. spectral data

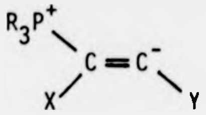
1,2-Diphosphoranes (90)



R	R'	δ^a			
OMe	Me	90.05	89.48(13)	88.87(13)	88.19
OMe	Ph	75.66	74.35(12)	72.94(12)	71.77
Ph	OMe	66.30	65.64(10)	64.82(10)	64.08
OEt	Ph	71.04	69.93(10)	68.51(10)	67.44

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; J_{PP} in Hz in parentheses, [^{2}H]Chloroform, 26 °C.

(1b; R = Ph; X,Y = CO_2Me). [See Introduction]

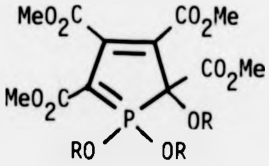


(1b)

More recently Tebby, Willetts, and Griffiths[50] have reported a preliminary study into the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate and have obtained n.m.r. evidence for a number of reactive intermediates. We have now studied this reaction in more detail and have extended the study to include the reaction of several dialkyl phosphonites.

2.1 The reaction of trialkyl phosphites with an excess of dimethyl acetylenedicarboxylate.

The reaction of a trialkyl phosphite with two molar equivalents of dimethyl acetylenedicarboxylate at room temperature in chloroform is very rapid, so that under normal circumstances the only signals observed in the ^{31}P n.m.r. spectrum of the resulting mixture are those in the region of δ_P 80-85 p.p.m. corresponding to the final product of the reaction, the 2H-1λ^5-phosphole, a cyclic ylide (91; R = Me, Et).



(91)

However, when the ^{31}P n.m.r. spectrum of the reaction mixture was run immediately after the phosphite and acetylene had been mixed an additional transient signal was observed at high field, at δ_P -37, -42, and -48 p.p.m. for the reactions using trimethyl, triethyl, and tri-isopropyl phosphite respectively, this being characteristic of compounds containing five co-ordinate phosphorus.[58] Since these signals clearly arose from a precursor of the cyclic ylides (91; R = Me, Et, Pr^i), attempts were made to slow the rate of rearrangement of these components so that they could be studied in more detail. Fortunately, it was found that the rate of rearrangement could be significantly slowed by using toluene as the solvent rather than chloroform. Thus, for example, by using toluene as the solvent and by mixing trimethyl phosphite with dimethyl acetylenedicarboxylate at 0 °C it was possible to obtain an initial spectrum which showed the high field component at δ_P -37 p.p.m. accounting for about 50% of the total ^{31}P n.m.r. signal.

However, attempts to slow the rate of rearrangement of the high field component by the use of low temperatures were even more dramatic. For example, when a solution of tri-isopropyl phosphite in toluene at -70 °C was added to a solution containing 2 molar equivalents of dimethyl acetylenedicarboxylate, also in toluene at -70 °C, the ^{31}P n.mr. spectrum of the resulting solution showed no significant reaction had occurred. Furthermore, even after 40 minutes at -70 °C there had been no significant reaction. The trimethyl and triethyl phosphites were slightly more reactive than the tri-isopropyl phosphite, but still relatively unreactive at low temperature. Thus, for example, at -50 °C the reaction between trimethyl phosphite and dimethyl acetylenedicarboxylate in toluene

TABLE 2

^{31}P N.m.r. spectral data

Trialkoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)-methylene]phosphoranes (92)

R	δ [a]
Me	59.4
	61.6
Et	54.1
	55.8
Pr^i	49.3
	51.0

[a] Shifts in p.p.m. from 85% phosphoric acid; [$^2H_8$]Toluene, -50 °C.

^{31}P N.m.r. spectra of trimethoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)-methylene]phosphorane (92; R = Me).

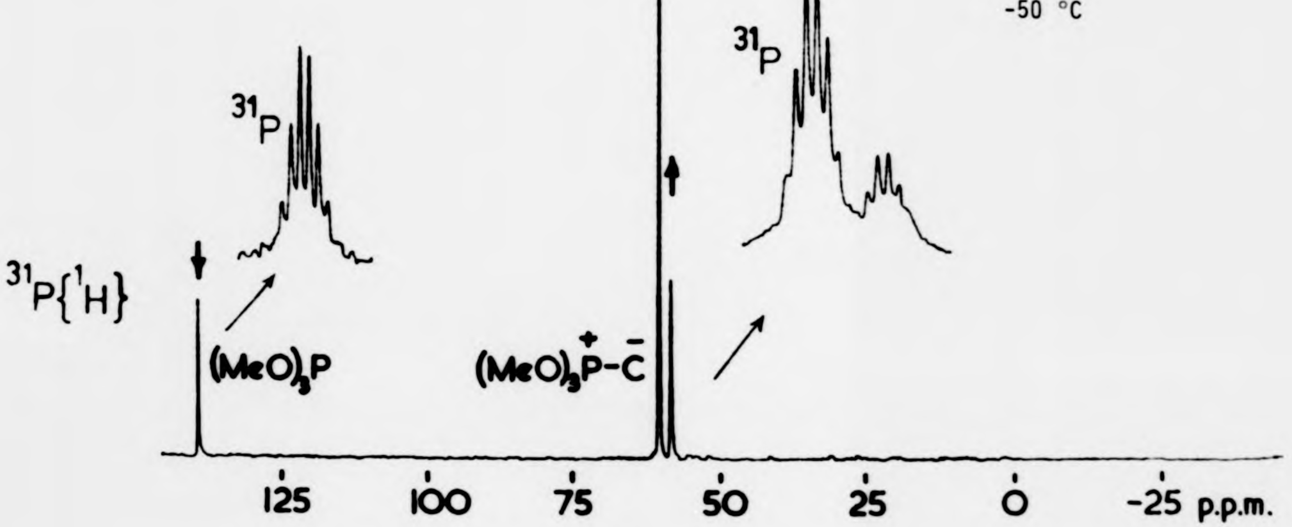
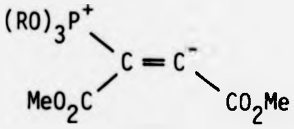


Plate 2

took about 2h. before the ^{31}P n.m.r. signals of the phosphite had disappeared from the spectrum. Moreover, the product formed at this time was not the precursor of the cyclic ylide (91; R = Me) giving the high field ^{31}P n.m.r. signal at δ_P -37 p.p.m. but one giving two signals at δ_P 59.4 and 61.6 p.p.m. (Plate 2). The same behaviour was also observed with triethyl and tri-isopropyl phosphite (Table 2).

Since the ^{13}C n.m.r. spectrum of the reaction mixtures after 2h. at -50 °C showed that no unreacted dimethyl acetylenedicarboxylate remained it was clear that these initially observed signals arose from an intermediate in which two molecules of acetylene had reacted with one molecule of the phosphite. No spectroscopic evidence for the formation of the proposed 1:1 intermediate (87) had thus been observed.

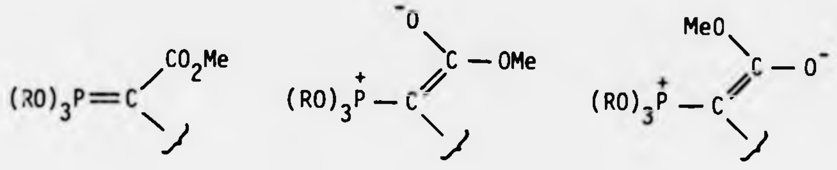


(87)

2.1.1. Studies on the 1:2 intermediate initially formed on the reaction of trialkyl phosphites with 2 molar equivalents of dimethyl acetylenedicarboxylate.

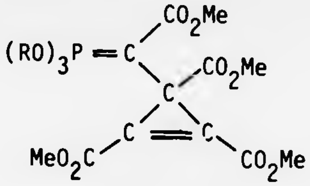
Since the initially formed 1:2 intermediates (92) were formed in essentially quantitative yield at low temperature it was possible to study these intermediates directly without any isolation being required. However, since it was found that a slight excess of the dimethyl acetylenedicarboxylate in the reaction mixture helped to ensure suppression of the formation of the 1,2-diphosphoranes (88), the ^{13}C n.m.r. studies were carried out on a reaction mixture which contained a slight excess of the acetylene.

A study of the ^{31}P n.m.r. spectrum of the initially formed 1:2 intermediates revealed several points of interest. Firstly, the intermediate or intermediates always gave rise to two signals in the ^{31}P n.m.r. spectrum in the region δ_P 49-62 p.p.m. [see Table 2], while the associated proton-coupled ^{31}P n.m.r. spectrum showed clearly that in all cases three alkoxy groups still remained attached to the phosphorus atom. These features suggested that the pairs of signals were due to the formation of ylides. Secondly, the relative intensities of these pairs of signals were found to be temperature dependent. Thus, for example, in the case of the reaction involving trimethyl phosphite the signal at δ_P 59.4 p.p.m. accounted for 40% of the total ^{31}P n.m.r. signal at -20 °C but, only 25% of the total signal at -60 °C. This effect was also shown to be reversible. The ratio was also found to vary depending on the particular trialkyl phosphite used in the reaction. For example, for tri-isopropyl phosphite the lower field signal at δ_P 51.0 p.p.m. accounted for over 80% of the ^{31}P n.m.r. signal about -50 °C and only 56% of the signal at -30 °C. It was therefore concluded that the pairs of signals arising from the 1:2 intermediates were in equilibrium. This type of behaviour is consistent with the presence of an ylide having an α-alkoxycarbonyl group.[5] We have previously seen in the case of the diphosphoranes (88) that in this type of compound there is restricted rotation about the bond from the α-carbon to the alkoxycarbonyl group due to the partial double bond character in this bond. The 1:2 intermediates therefore appeared to contain the partial structure (93).



(93)

This in turn suggested that the structure of the 1:2 intermediate was that of the trialkoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)methylene]phosphorane (92).



(92)

The ^{13}C n.m.r. spectrum of the initially formed 1:2 intermediates (92) was consistent with this proposed structure. Thus, the ^{13}C n.m.r. spectrum of the ylide (92; R = Me) (Plate 3) (Table 3) showed the α-carbon signal both at high field and also possessing the characteristically large $^{1}J_{PC}$ coupling (225 Hz) which we have observed in a number of other quasi-phosphonium ylides of this type. Furthermore, the symmetrical nature of the cyclopropene ring was clearly shown by both the coincidence of the two γ-carbons (at δ_C 115.99 p.p.m. in the major rotamer) and the two γ-carbonyl resonances (at δ_C 158.89 p.p.m. in the major rotamer).

^{13}C N.m.r. spectrum of trimethoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)methylene]-phosphorane (92; R = Me) (proton decoupled).

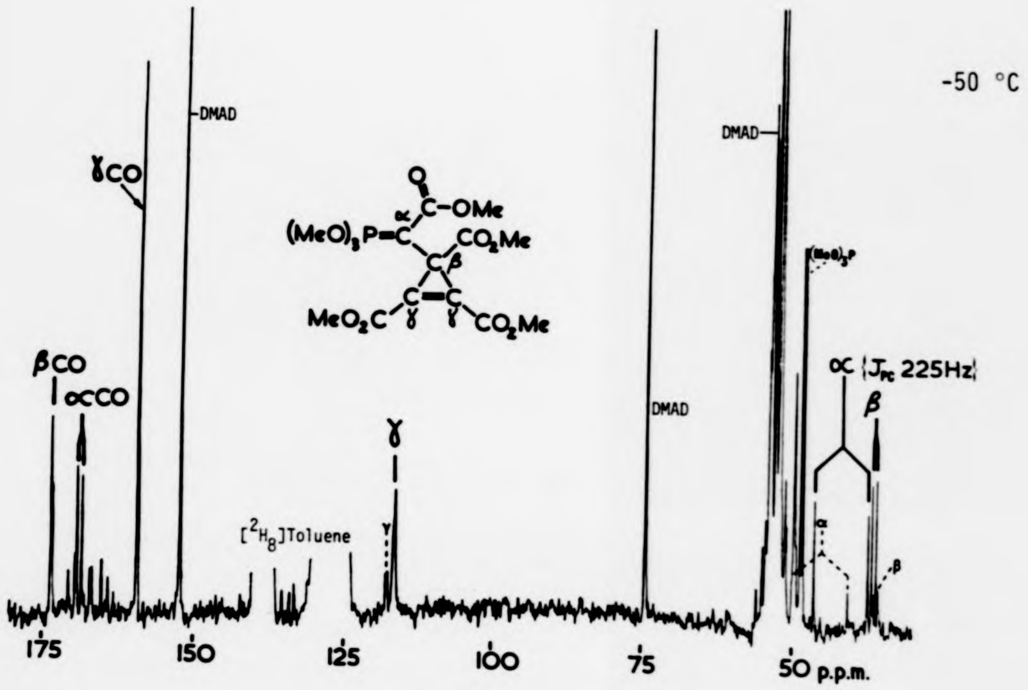


Plate 3

TABLE 3

^{13}C N.m.r. spectral data

Trimethoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)-methylene]phosphorane (92; R = Me).

	δ^{a}	
R	53.77(4)	
α-C	42.02(225)	44.90(225)[b]
β-C	36.55(18)	36.19(17)[b]
γ-C	115.99	116.70[b]
C=O	158.89	
	158.89	
	168.44(21)	
	173.04(5)	
OMe	49.90	
	52.48	
	52.48	
	52.48	

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [$^2H_8$]Toluene, -50 °C.

[b] Minor isomer.

Mechanism of formation

It is interesting to consider the mechanism of formation of the ylides (92) since two mechanisms appear possible. In the first (see Fig. 18) we can envisage the reaction of the "anionic form" of the 1:1 intermediate (87) attacking the electrophilic acetylene to produce an intermediate (94) which then cyclises to give the desired cyclopropene system (92).

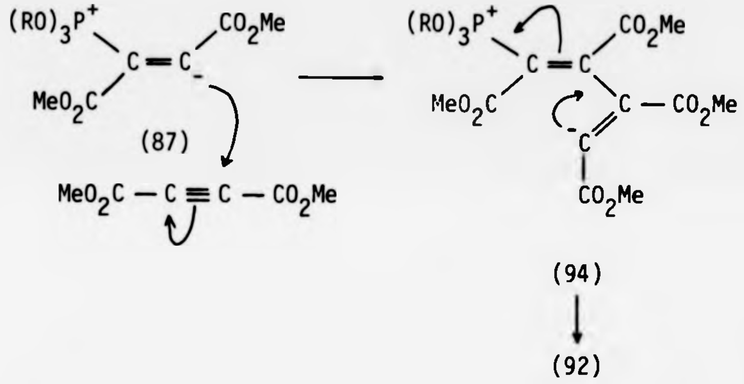


Fig. 18

In the second mechanism we can regard the 1:1 intermediate in its "carbenoid form" (87) undergoing an intermolecular carbene insertion into the carbon-carbon triple bond (Fig. 19).

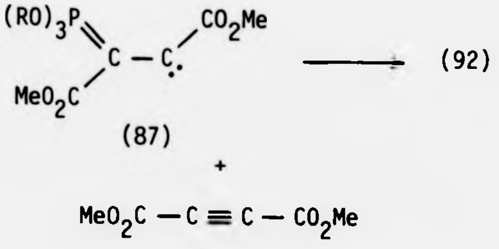
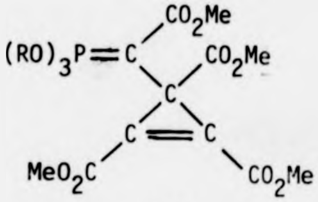


Fig. 19

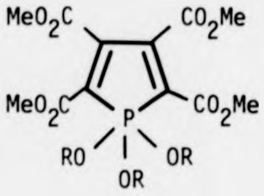
Unfortunately, however, it has proved to be difficult to obtain evidence to distinguish between these two mechanisms. Any components which could be added to the reaction mixture to intercept the intermediate (94) would also intercept the initially formed 1:1 intermediate (87) hence preventing the formation of the intermediate (94).

2.1.2. Studies on the 1:2 intermediate giving a high field ^{31}P n.m.r. signal formed in the reaction of trialkyl phosphites with a 2 molar equivalent of dimethyl acetylenedicarboxylate.

Although the ylides (92) were reasonably stable at temperatures below about -50 °C, they readily underwent rearrangement at higher temperatures. The rate of rearrangement was found to be dependent not only on the temperature of the solution but also on the nature of the alkoxy groups on the phosphorus. Thus the more bulky the alkoxy group the less readily it rearranged. However, after several minutes at about -20 °C even the ylide (92; $R = Pr^i$) had completely rearranged. At this temperature the rearrangement product was the component previously mentioned which gave a high field signal in the ^{31}P n.m.r. spectrum and which had been shown to be the precursor of the cyclic ylide (91). The ^{31}P n.m.r. shifts and multiplicities of the rearrangement products indicated that they were five co-ordinate phosphoranes which still had three alkoxy groups attached to the phosphorus atom. This was consistent with the formation of the η^5-phospholes (95). This structure was confirmed by the ^{13}C n.m.r. spectra which showed clearly the symmetrical nature of η^5-phospholes (95).



(92)



(95)

The ^{13}C n.m.r. spectrum of the η^5-phosphole (95; R = Me) is shown in Plate 4, and the n.m.r. data is given in Table 4, together with that for the ethyl analogue (95; R = Et). The n.m.r. data for the η^5-phosphole (95; R = Pr^i) is given in the Experimental section. It can be seen from the data in Table 4 that the α-carbons are now at considerably lower field (by about 100 p.p.m.) and that the $^1J_{PC}$ couplings are significantly smaller (135 - 143 Hz) than those observed in the ylides (92; R = alkyl) (Table 3). The equivalence of the three alkoxy groups on the phosphorus shows that pseudorotation is still very rapid at these temperatures. Indeed, even at temperatures down to about -90 °C no sign of significant slowing of the pseudorotation process was observed.

Mechanism of rearrangement

It is interesting to consider the mechanism of the rearrangement of the ylides (92) to the η^5-phospholes (95) because once again two mechanisms are possible. We can consider either a concerted mechanism, such as that shown in Fig. 20 or one which involves the initial formation of an ionic species (94) (see Fig. 21).

^{13}C N.m.r. spectrum of tetramethyl 1,1,1-trimethoxy-n^5-phosphole-2,3,4,5-tetracarboxylate (95; R = Me) (proton decoupled).

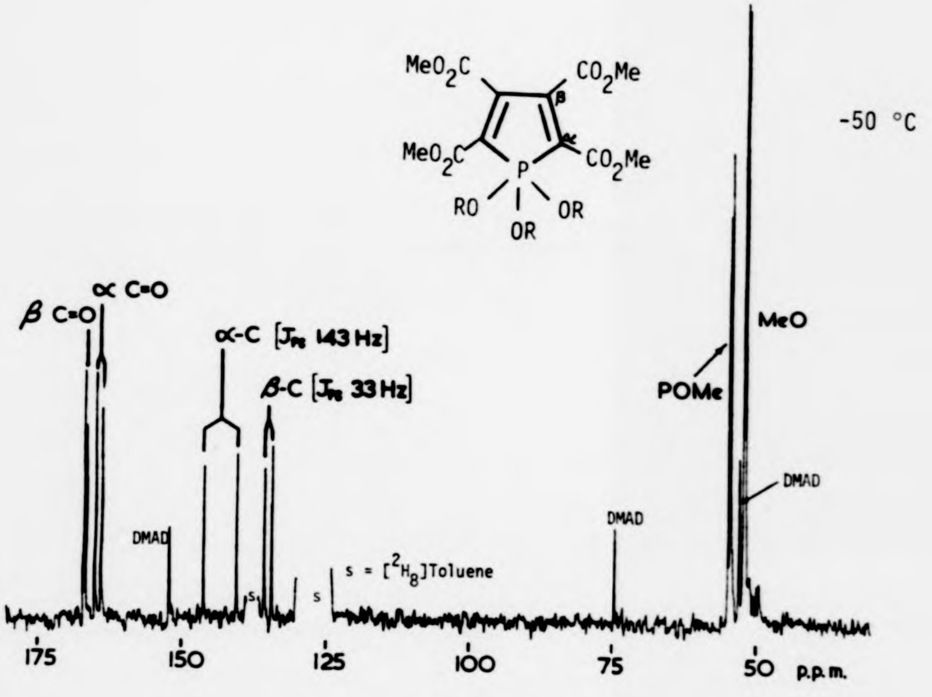


Plate 4

TABLE 4

N.m.r. spectral data

Tetramethyl 1,1,1-Trialkoxy-n^5-phosphole-2,3,4,5-tetracarboxylates (95).

	R = Me	R = Et
$\delta(^{31}P)$[a]	-37.4 [b]	-41.84 [c]
	(dec, 14)	(sept, 9)
$\delta(^{13}C)$[d]		
R	54.76(11)[e]	16.34(9)[f]
		63.34(10)
α-C	142.85(143)	144.25(135)
β-C	134.61(33)	133.83(32)
C=O	164.01(27)	163.88(77)
	166.32(9)	166.93(9)
OMe	51.96	52.26
	52.20	52.67

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; J_{PH} in Hz in parentheses.

[b] [$^2H_8$]Toluene, -50 °C.

[c] [^2H]Chloroform, 26 °C.

[d] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses.

[e] [$^2H_8$]Toluene, -15 °C.

[f] [^2H]Chloroform, -30 °C.

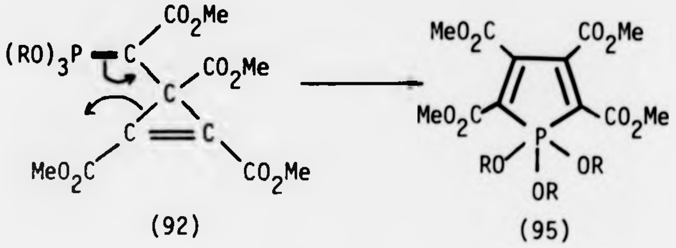


Fig. 20

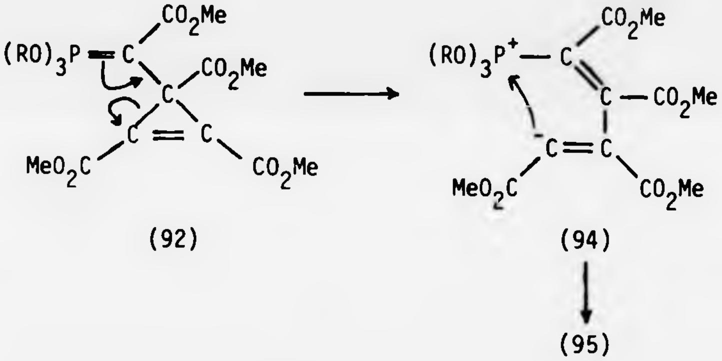
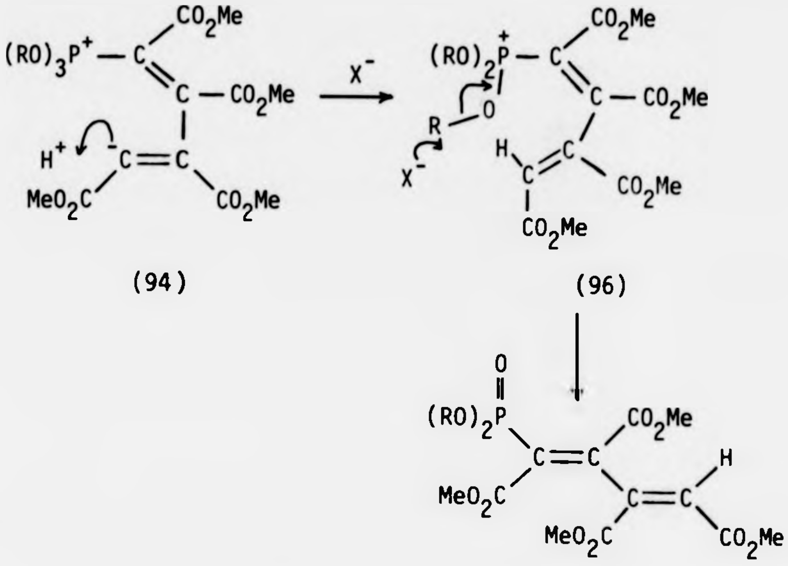


Fig. 21

Efforts were therefore made to ascertain which of these two mechanisms was involved. If the ionic species (94) was present in the reaction mixture then it was felt that it would be possible to trap this intermediate by having a proton donor present. Under these circumstances we might expect the anion (94) to be protonated and the resulting quasi-phosphonium salt (96) to then undergo dealkylation to give the phosphonate (97).



(94)

(96)

(97)

If on the other hand, the presence of the proton donor was found to have no effect on the rearrangement of the ylide (92), we could conclude that the rearrangement proceeded via the concerted mechanism (Fig. 20).

It was felt that acetic acid might prove to be a suitable proton donor for this study. However, it was first necessary to check that the resulting n^5-phosphole (95) would be unaffected by this reagent. A sample of the n^5-phosphole (95; R = Me) was therefore prepared at -10 °C and treated with acetic acid at this temperature. This appeared to have no impact on the n^5-phosphole (95; R = Me) which rearranged normally, even in the presence of the acetic acid,at room temperature to give the cyclic ylide (91; R = Me). However, when the acetic acid was added to a sample of the ylide (92; R = Me) at -70 °C and the sample then allowed to warm up slowly to room temperature, the major product was not the cyclic ylide

(91; R = Me) but the phosphonate (97) at δ_P 10.6 p.p.m. (septet, $^3J_{PH}$ 12 Hz) in the ^{31}P n.m.r. spectrum. A pure sample of this material was obtained by preparative thin layer chromatography on silica gel using ethyl acetate as the eluant. This material gave the correct combustion analysis and molecular ion (as indicated by mass spectroscopy), and the ^{13}C n.m.r. spectrum (Table 5) was consistent with the proposed structure. Interestingly, only one stereoisomer of (97) seems to be formed.

Although the presence of the ionic species (94) in the reaction mixture was confirmed, it is probably unwise to conclude that this demonstrates that the rearrangement mechanism proceeds via the ionic species (94) (Fig. 21). Before this could be done it would be necessary to establish that the ionic species (94) and the ylide (92) were not in equilibrium. If an equilibrium were to exist this would rapidly lead to the formation of the observed phosphonate (97) in the presence of a proton donor independently of any mechanism leading to cyclic ylide (91; R = Me) formation.

2.1.3 Study of the cyclic ylides formed in the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate.

Although the η^5-phospholes (95) were stable at temperatures below about -10 °C they readily rearranged to the cyclic ylides (91) at higher temperatures. At room temperature the rearrangement was complete within 15 minutes. The ^{13}C n.m.r. spectra of the cyclic ylides (91; R = Me, Et, Pr^i) formed in the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate (Table 6)(Plate 5; R = Me) clearly show that the three alkoxy groups originally on the phosphorus in the η^5-phosphole (95) are now no longer equivalent. Indeed, one of the alkoxy groups, the one which has

TABLE 5

^{13}C N.m.r. spectral data.

1,2,3,4-Tetramethoxycarbonyl-1-(dimethoxyphosphinyl)-1,3-butadiene (94).

	δ^{a}
R	53.47(6)
α-C	134.47(71)
β-C	139.87(7)
γ-C	141.38(5)
δ-C	129.46[b]
C=O	162.51(26)
	163.89
	164.22
	165.08(11)
OMe	52.18
	52.91
	53.04
	53.16

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C .

[b] From the ^{13}C n.m.r. proton-coupled spectrum: d, $^{1}J_{CH}$ 171 Hz.

TABLE 6

^{13}C N.m.r. spectral data

Tetramethyl 1,1,2-Trialkoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91).

	R = Me	R = Et	R = Pr^i
δ[a]			
R	54.45(7)[b]	15.54[c]	24.15-23.47[b,d]
	57.53(7)	15.99(7)	24.39(2)
	58.49(8)	15.99(7)	
		62.49(7)	71.28(10)
		68.06(9)	78.29(10)
		69.15(9)	79.10(9)
α-C	63.81(139)	65.11(139)	66.52(139)
β-C	162.62(38)	159.37(38)	158.65(38)
γ-C	100.28(27)	100.01(26)	101.13(25)
δ-C	83.75(113)	82.46(114)	80.55(120)
C=0	163.29(9)	163.37(16)	164.10(17)
	163.45(17)	163.61(9)	164.09(11)
	165.59(24)	166.23(24)	166.69(25)
	166.93	167.00	167.98(2)
OMe	50.54	50.68	50.39
	50.89	51.21	51.07
	52.01	52.45	52.27
	52.49	52.75	52.34

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses.

[b] [^{2}H]Chloroform, 26 °C.

[c] [$^2H_8$]Toluene, 50 °C.

[d] Multiple signals.

^{13}C N.m.r. spectrum of tetramethyl 1,1,2-trimethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Me) (proton decoupled).

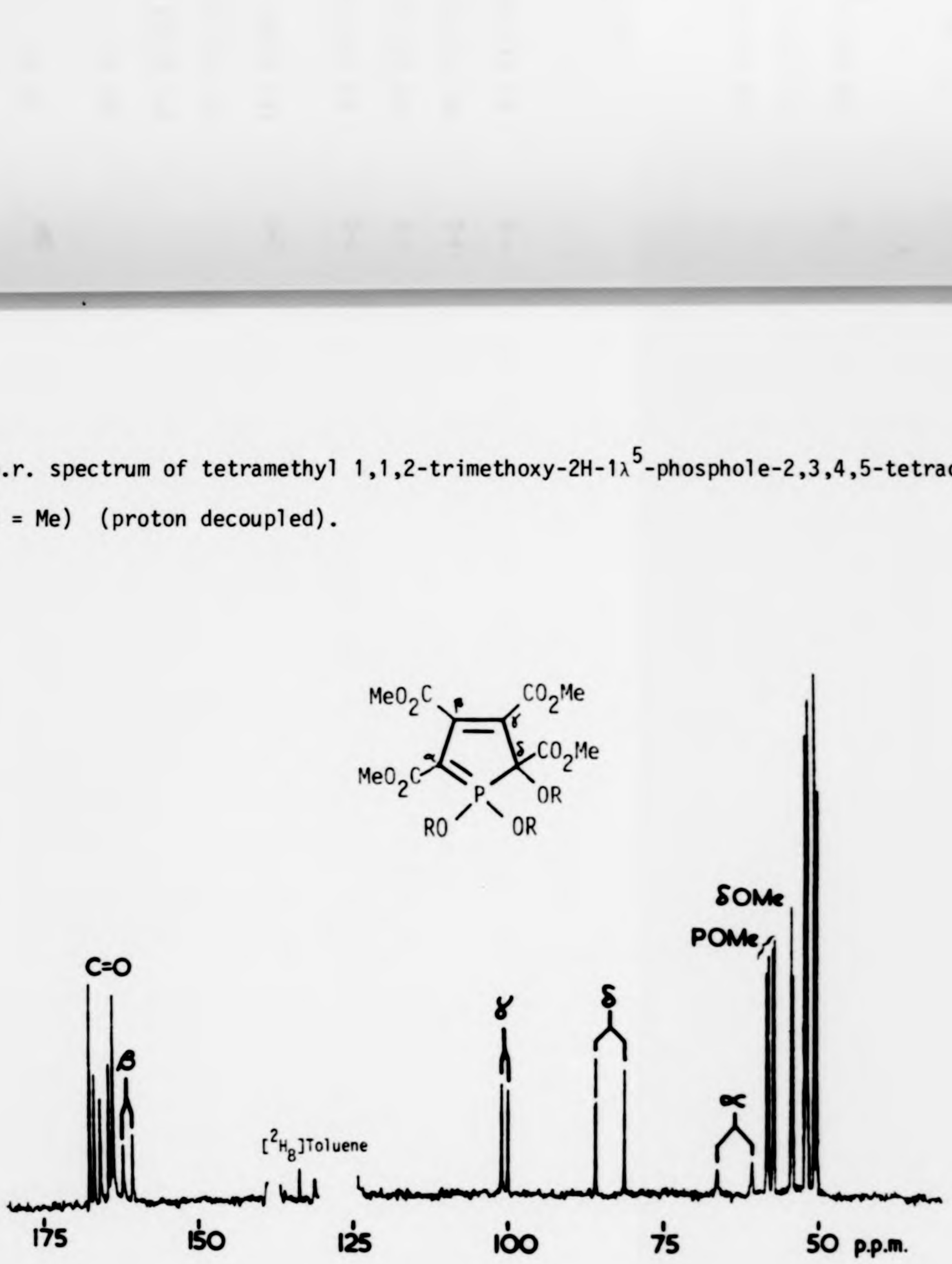


Plate 5

migrated to the adjacent δ-carbon has a significantly different shift from those still attached to the phosphorus. The presence of only two alkoxy groups on the phosphorus is also confirmed by the multiplicity of the proton-coupled ^{31}P n.m.r. signals of the cyclic ylides (Table 7).

At low temperatures the ^{31}P n.m.r. signal for the cyclic ylides sharpen to reveal four separate resonance lines (see Table 7) (Plate 6; R = Me) which is consistent with a structure where one might predict some restricted rotation about the bond to the α- and γ-methoxycarbonyl groups (Fig. 22).

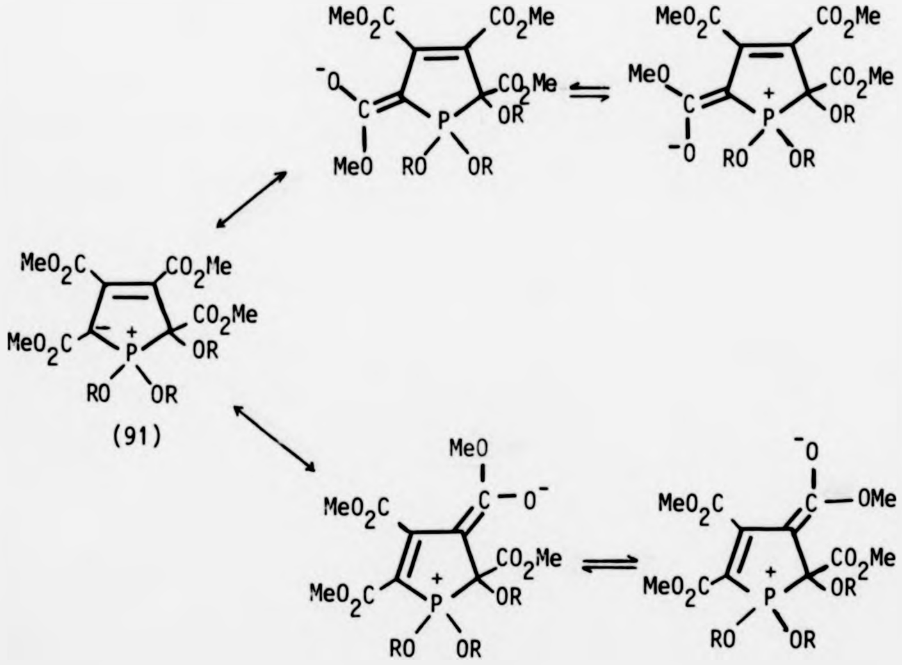


Fig. 22

TABLE 7

^{31}P N.m.r. spectral data

Tetramethyl 1,1,2-Trialkoxy -2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91).

	R = Me	R = Et	R = Pr^i
δ[a]	84.40	80.51	75.61 [b]
	(sept, 12)	(quin, 7)	(t, 7)[c]
	85.9 [d]	82.0 [d]	78.44 [e]
	85.3	81.38	77.86
	83.1	79.89	75.75
	82.4	79.16	75.10

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; J_{PH} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] δ(^{31}P) 76.48 p.p.m., [$^2H_8$]Toluene, 26 °C.

[c] Broad signal.

[d] [^{2}H]Chloroform, -50 °C.

[e] [$^2H_8$]Toluene, -50 °C.

Temperature dependence of the ^{31}P n.m.r. spectrum (proton decoupled) of tetramethyl 1,1,2-trimethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Me).

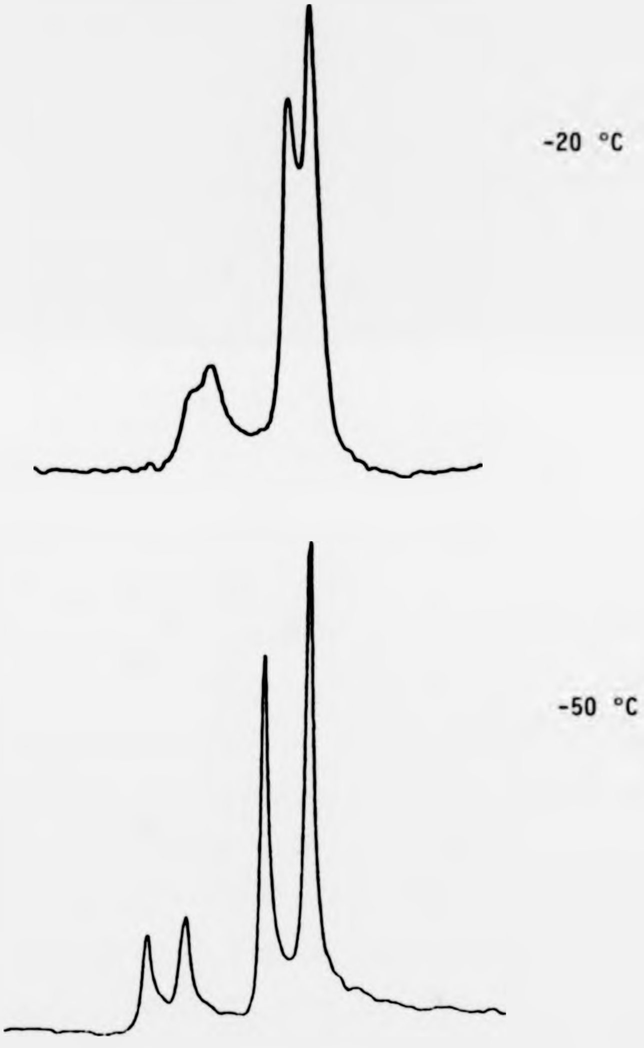
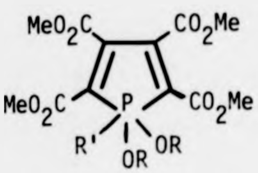


Plate 6

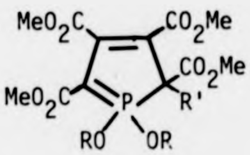
The cyclic ylides (91) were in general sufficiently stable to be isolated without the need for special precautions. The cyclic ylides (91; R = Et and Pr^i) were eventually isolated in a pure state as white crystals by triturating with ether the oil obtained on removal of the solvent from the reaction mixture. However, considerable difficulties were experienced with the isolation of the cyclic ylide (91; R = Me). Trituration was unsuccessful and attempts to chromatograph the crude cyclic ylide on alumina, silica and florisil all led to retention of the cyclic ylide on the stationary phase. The pure cyclic ylide (91; R = Me) was eventually obtained from a particularly clean preparation after removing any volatile components under vacuum (0.05 mm Hg). Burgada *et al.*[35] have recently reported the preparation and isolation of the cyclic ylide (91; R = Me) as a solid which they claimed to be able to recrystallise from carbon tetrachloride.

2.2 The reaction of dialkyl phosphonites with an excess of dimethyl acetylenedicarboxylate.

Having investigated the reaction of some trialkyl phosphites with a 2 molar equivalent of dimethyl acetylenedicarboxylate it was of interest to extend this study to some dialkyl phosphonites to see how significant an effect this change would have on the stabilities of the intermediates formed in the reaction. Furthermore, if the dialkyl phosphonites were found to react by a route analogous to that observed in the case of the trialkyl phosphites it would be of interest to see which of the substituents on the phosphorus migrated when the η^5-phospholes, (98; R = alkyl, R' = aryl) and (98; R = R' = alkyl), rearranged. In other words, would it be the cyclic ylides (99; R = alkyl, R' = aryl) and (99; R = R = alkyl) or the cyclic ylides (100; R = alkyl, R' = aryl) and (100; R = R = alkyl) which were produced.



(98)



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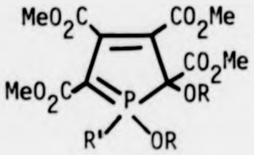
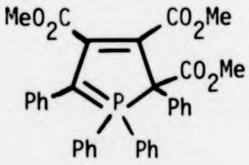
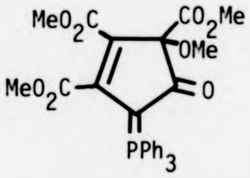


(100)

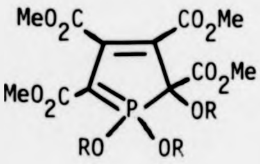
Additionally, in the previous work on the reaction of triphenylphosphine with dimethyl acetylenedicarboxylate, two products, the cyclic ylide (80) and the exocyclic ylide (81), had been isolated.[40,48,49] This contrasts with our studies of the reaction of the trialkyl phosphites with dimethyl acetylenedicarboxylate which led to the formation of the cyclic ylides (91), but not the exocyclic ylides (101; R = alkyl, R' = O-alkyl). It was thus of interest to see whether the exocyclic ylides (101; R = alkyl, R' = aryl) were formed in the reactions involving the dialkyl phosphonites.



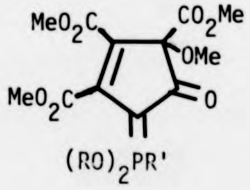
(80)



(81)



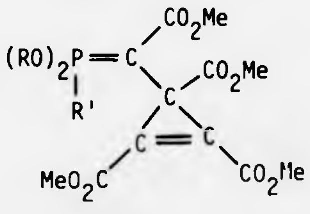
(91)



(101)

2.2.1 The reaction of dialkyl phenylphosphonites with an excess of dimethyl acetylenedicarboxylate.

In general the reactions of the dialkyl phenylphosphonites with dimethyl acetylenedicarboxylate followed an analogous route to that observed in the trialkyl phosphite reactions, [see earlier Discussion]. However, the phosphonites were found to react more readily with the dimethyl acetylenedicarboxylate than the trialkyl phosphites and, furthermore, the intermediates formed were less stable than the corresponding ones from the trialkyl phosphites. Thus, for example, while the reaction of diethyl phenylphosphonite with dimethyl acetylenedicarboxylate, at low temperature in toluene, led to the formation of the ylide (102; R = Et, R' = Ph) in almost quantitative yield, the reaction time of approximately 30 min. at -70 °C was considerably shorter than the 1-2 h. at -50 °C observed in the reaction of trimethyl phosphite at similar concentrations.



(102)

The rate of formation of the ylide (102; R = Me, R' = Ph) was however, considerably slower than that for ylide (102; R = Et, R' = Ph), by a factor of about four. This significant lower reactivity cannot be completely explained by the reduced nucleophilicity of the dimethyl phenylphosphonite relative to the diethyl phenylphosphonite as we found the two phosphonites to exhibit similar reactivity towards methyl iodide.

As with the ylides (92; R = alkyl) previously studied, those from the dialkyl phenylphosphonites (102; R = alkyl, R' = phenyl) were observed as two rotamers in the ^{31}P n.m.r. spectrum (Table 8). These ^{31}P n.m.r. signals were still within the region characteristic of alkylidenephosphoranes,[53] but were significantly further downfield of those signals observed for the ylides (92; R = alkyl) from the trialkyl phosphites.

Once again the ^{13}C n.m.r. spectrum of the ylide (102; R = Et, R' = Ph) (Table 9) clearly shows the presence of both rotamers. The α-carbons at δ_C 40.78 (major) and 47.21 (minor) p.p.m. both show characteristically high $^1J_{PC}$ values of 229 and 203 Hz respectively. Also, the two γ-carbons are once again coincident due to the symmetry of the cyclopropene ring and are observed in the appropriate region of the spectrum, δ_C 116.49 (major) and 118.51 (minor) p.p.m.

Interestingly the formation of (102; R = Et, R' = Ph) occurs via the less stable rotamer, that giving a signal at $\delta(^{31}P)$ 64.7 p.p.m. since this is the only signal seen during the early part of the reaction. However, as the reaction proceeds this is converted into the other rotamer so that after about 2 h. at -70 °C the major signal is that at δ_P 65.8 p.p.m. (approx. 70% by ^{31}P n.m.r.).

The reduced stability of the ylide (102; R = Et, R' = Ph) over that formed from the trialkylphosphites (92) was clearly shown by the observation that rearrangement of the ylide (102; R = Et, R' = Ph) had occurred and even at -70 °C. After 1.5 h. at -70 °C about 30% of the ylide (102; R = Et, R' = Ph) had undergone rearrangement to give the η^5-phosphole (98; R = Et, R' = Ph).

TABLE 8

^{31}P N.m.r. spectral data

Dialkoxyphenyl[methoxycarbonyl-(1,2,3-trimethoxycarbonylcyclopropenyl)-methylene]phosphoranes (102).

R	$\delta^{a,b}$
Me	73.3
	74.5
Et	64.7
	65.8

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference.

[b] [$^2H_8$]Toluene, -70 °C.

TABLE 9

^{13}C N.m.r. spectral data

Dialkoxyphenyl[methoxycarbonyl-(1,2,3-trimethoxycarbonylcyclopropenyl)methylene]phosphorane (102; R = Et, R' = Ph).

	δ^{a}
R	16.0^{b}
	61.9^{b}
R'	c
α-C	$40.78(229)^{d}$
β-C	$35.93(14)^{e}$
γ-C	116.5^{b}
C=O	158.88
	159.02
	168.78(27)
	173.41(4)
OMe	49.22
	52.21
	52.21
	52.21

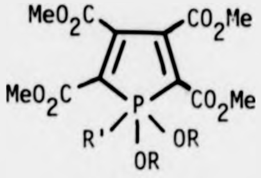
[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [$^{2}H_8$]Toluene, -70 °C.

[b] Broad signal.

[c] Signals obscured by solvent resonance.

[d] Minor rotamer 47.21(203).

[e] Minor rotamer 118.51 .



(98)

At -50 °C, the temperature previously used to prepare and study the ylide (92; R = Me), the rearrangement of the ylide (102; R = Et, R' = Ph) was complete in less than 30 minutes. The n^5-phosphole (98; R = Et, R' = Ph) was observed as a characteristically high field signal at $\delta(^{31}P)$ -34.0 p.p.m. once again somewhat downfield relative to the corresponding n^5-phospholes (95; R = alkyl) from the trialkyl phosphites (Table 4). The analogous n^5-phosphole (98; R = Me, R' = Ph) was also observed at high field (δ_P -31.9 p.p.m.) and showed an ill-resolved 9 line signal ($^3J_{PH}$ 15 Hz) in the proton--coupled ^{31}P n.m.r. spectrum due to coupling with the six methoxy protons and the two *ortho*-protons on the phenyl substituent on the phosphole.

Once again the ^{13}C n.m.r. spectrum of the n^5-phosphole from the dialkyl phenylphosphonite (Table 10) reflected the symmetrical nature of the molecule and was consistent with the proposed structure.

During the rearrangement of the ylide (102; R = Et, R' = Ph) at -50 °C to the corresponding n^5-phosphole (98; R = Et, R' = Ph) it was very difficult to avoid further rearrangement of the n^5-phosphole (98; R = Et, R' = Ph) to give the cyclic ylide (99 or 100; R = Et, R' = Ph). Indeed at -50 °C rearrangement of the ylide (102; R = Et, R' = Ph) to the cyclic ylide (99 or 100) via the n^5-phosphole (95; R = Et, R' = Ph) was more than 90% complete

TABLE 10

N.m.r. spectral data

Tetramethyl 1,1-Diethoxy-1-phenyl-n^5-phosphole-2,3,4,5-tetracarboxylate (98; R = Et).

$\delta(^{31}P)$[a]		-34.0
$\delta(^{13}C)$[b]		
	R	16.28(8)
		62.06(10)
	R'	c
	α-C	147.60(98)
	β-C	134.18(26)
	C=O	163.81(22)
		167.58(10)
	OMe	51.72
		52.09

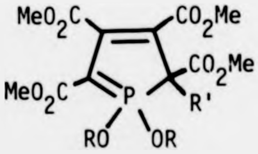
[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; $[^2H_8]$Toluene, -70 °C.

[b] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parenthesis; $[^2H_8]$Toluene, -70 °C.

[c] Signals obscured by solvent resonances.

after about 1 h., again highlighting the reduced stability of the intermediates produced in the dialkyl phenylphosphonite reaction.

Although the rearrangement of the n^5-phosphole was shown by n.m.r. spectroscopy to give cyclic ylides (99 or 100) analogous to those prepared from the trialkyl phosphites (95), it was important to assess which of the groups had migrated during the rearrangement. Charrier, Mathey et al.[70] have reported that the coordination state of the phosphorus has a profound influence on the migratory aptitude of its substituents. They found that the migratory aptitude increased in the order tetra coordinate P < tri coordinate P << penta coordinate P. They also concluded that the migratory aptitude of the substituents on phosphorus followed the trend OR << Ph << H. The low migratory aptitude of the alkoxy substituents on phosphorus was accounted for by considering the relative strength of the P-O bond over the P-C and P-H bonds. On the basis of this we would have expected therefore that rearrangement of the n^5-phospholes (98; R = Me, Et; R' = Ph) would have resulted in the migration of the phenyl group to give the 2H-1λ^5-phosphole (99; R = Me, Et, R' = Ph) and not its isomer (100; R = Me, Et, R' = Ph).



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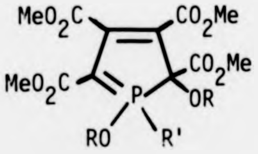


(100)

However, it was clear from the n.m.r. spectra of the resulting 2H-1λ^5-phospholes that the structure was that of (100; R = Me, Et, R' = Ph) and not that of (99; R = Me, Et, R' = Ph), this having formed as a result of the 1,5-migration of an alkoxy group during rearrangement of the n^5-phospholes (98; R = Me, Et; R' = Ph). Thus, for example, the multiplicity of the proton-coupled ^{31}P n.m.r. spectrum of the 2H-1λ^5-phospholes (100; R = Me, R' = Ph)δ_P 86.1 p.p.m. $^3J_{PH}$ 12 Hz, and (100; R = Et, R' = Ph)δ_P 83.9 p.p.m. $^3J_{PH}$ 14 Hz, a broadened quartet and triplet respectively, clearly showed the presence of only one alkoxy group with proton-coupling to phosphorus. The broadening being due to a further smaller coupling to phosphorus from the two *ortho*-protons on the phenyl substituent.

Low temperature ^{31}P n.m.r. spectroscopy revealed the presence of four separate resonance signals (Table 11) for the 2H-1λ^5-phospholes (100; R = Me, Et, R' = Ph). This is consistent with the proposed structure in which restricted rotation about the bond to the *α*- and *γ*-methoxycarbonyl groups can occur and this phenomena was previously noticed in the ^{31}P n.m.r. spectra of the 2H-1λ^5-phospholes (91; R = Me, Et, Pr^i) prepared from the trialkyl phosphites (Table 7).

The ^{13}C n.m.r. spectra of the 2H-1λ^5-phospholes (100; R = Me, Et, R' = Ph) (Table 12) are consistent with the proposed structure and that for the 2H-1λ^5-phosphole (100; R = Et, R' = Ph) (Plate 7) and clearly shows that the two ethoxy groups originally on the phosphorus are no longer equivalent. The ^{13}C spectra of the 2H-1λ^5-phospholes (100; R = Me, Et, R' = Ph) (Table 12) also show a large $^1J_{PC}$ coupling to the *ipso*-carbon of the phenyl substituent, confirming that the phenyl substituent is still attached to phosphorus. The characterisation of the 2H-1λ^5-phospholes (100; R = Me, Et, R' = Ph)

TABLE 11

^{31}P N.m.r. spectral data.

Tetramethyl 1,2-Dialkoxyl-1-phenyl-2H-1λ^5-phosphole-2,3,4,5--tetracarboxylate (100).

	R=Me	R=Et
δ[a]	86.1[b]	83.9[b]
		85.80[c]
		85.17
		83.60
		82.69

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference.

[b] [^{2}H]Chloroform, 26 °C.

[c] [^{2}H]Chloroform, -50 °C.

TABLE 12

^{13}C N.m.r. spectral data

Tetramethyl 1,2-Dialkoxy-1-phenyl-2H-$1\lambda^5$-phosphole-2,3-4,5-tetracarboxylate (100; R' = Ar).

δ^a		R=Et	R=Me
	R	14.59	53.44(8)
		16.11(7)	56.15(7)
		61.52(5)	
		66.75(7)	
	R'	120.35(125)	119.57(126)
		128.42(14)	128.50(13)
		133.29(11)	133.18(11)
		134.06(3)	134.18(3)
	α-C	63.01(140)	63.17(135)
	β-C	160.91(29)	161.79(28)
	γ-C	101.94(19)	101.16(19)
	δ-C	85.40(85)	85.35(86)
	C=O	163.43(13)	163.47(13)
		164.09(11)	164.07(10)
		166.31(19)	166.19(19)
		167.26	167.15
	OMe	50.53	50.67
		51.16	51.26
		52.38	52.47
		52.79	52.84

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

^{13}C N.m.r. spectrum of tetramethyl 1,2-diethoxy-1-phenyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R = Et, R' = Ph) (proton decoupled).

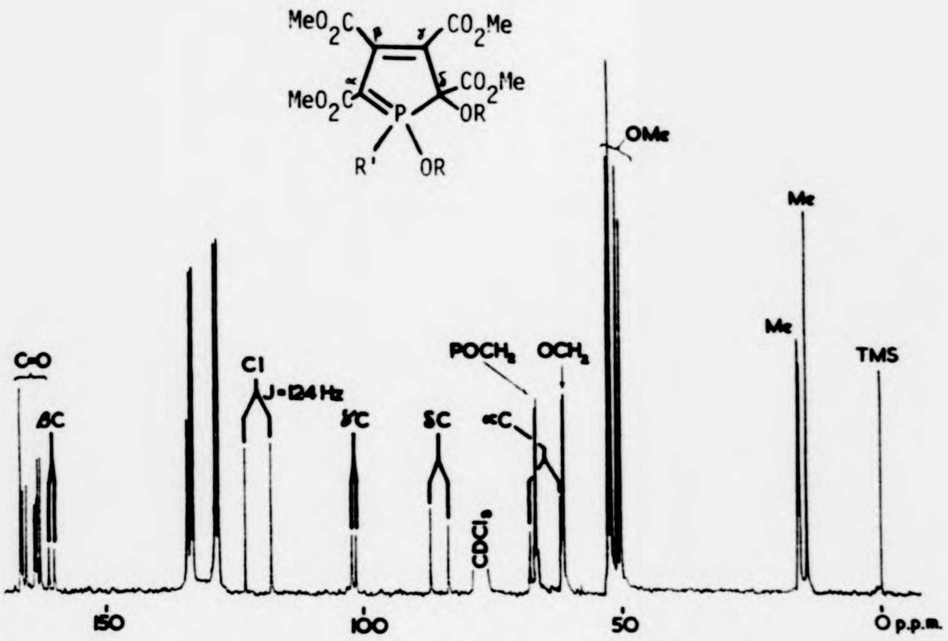
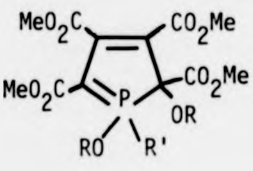


Plate 7

(Table 12) was aided by the similarity of their spectra with those of the 2H-1λ^5-phospholes (91; R = alkyl). No sign of the exocyclic ylide (101; R = alkyl, R' = phenyl) was observed in the reaction of the dialkyl phenylphosphonites with excess dimethyl acetylenedicarboxylate.



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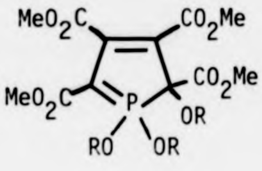

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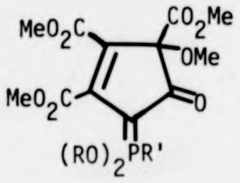


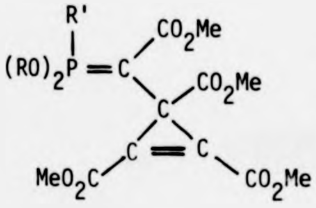
(101)

2.2.2 The reaction of dimethyl methylphosphonite with an excess of dimethyl acetylenedicarboxylate.

Dimethyl methylphosphonite [For preparative details see Experimental Section] was found to be even more reactive towards dimethyl acetylenedicarboxylate than the corresponding dialkyl phenylphosphonites and, the intermediates formed during the reaction even less stable. The formation of the ylide (102; R,R' = Me) δ(^{31}P) 85.1 and 86.8 p.p.m. at -70 °C was always accompanied by the formation of the n^5-phosphole (98; R,R' = Me) δ(^{31}P) -34.3 p.p.m. and a small quantity of the 2H-1λ^5-phosphole (100; R,R' = Me). Indeed, the rearrangement of the ylide (102; R,R' = Me) could not be prevented during the initial stages of the reaction, during the mixing of the phosphonite with the dimethyl acetylenedicarboxylate, despite the use of very low temperatures. However, once formed the mixture of the intermediates was reasonably stable at -70 °C with little change in the ^{31}P n.m.r. spectrum over 2 h. except for a change in the ratio of the rotamers of the ylide (102; R,R' = Me).

This instability of the intermediates did not allow conditions to be established for the selective preparation of the n^5-phosphole (98; R,R' = Me) as the conditions required to allow rearrangement of the ylide (102; R,R' = Me) to the n^5-phosphole (98; R,R' = Me) also led to the subsequent rearrangement to the cyclic ylide (100; R,R' = Me). The result of this was that the optimum conditions for the preparation of the n^5-phosphole (98; R,R' = Me) gave a mixture in which the n^5-phosphole accounted for about 20% of the total ^{31}P n.m.r. signal.

The 2H-1λ^5-phosphole (100; R,R' = Me) could however be obtained pure in good yield (70%). The ^{13}C n.m.r. spectrum of this material (Table 13) confirms the structure as being the 2H-1λ^5-phosphole (100; R,R' = Me) in which the 1,5-migration of an alkoxy group from phosphorus to carbon has occurred.



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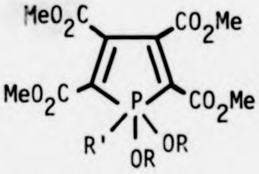

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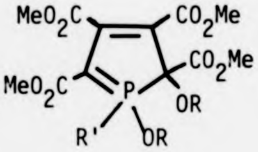


(100)

3. THE USE OF SULPHUR TO TRAP THE 1:1 INTERMEDIATE FORMED IN THE REACTION OF TRIMETHYL AND TRIETHYL PHOSPHITE WITH DIMETHYL ACETYLENEDICARBOXYLATE.

It has been previously reported that the 1:1 intermediate (29), formed from the reaction of triphenylphosphine with dimethyl

TABLE 13

N.m.r. spectral data

Tetramethyl 1,2-Dimethoxy-1-methyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R,R' = Me).

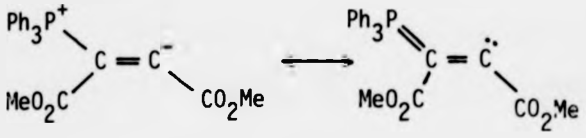
$\delta(^{31}P)$[a]		96.2[b]
		96.9
$\delta(^{13}C)$[c]	R	54.22(8)
		55.50(7)
	R'	6.87(86)
	α-C	61.10(140)
	β-C	161.17(27)
	γ-C	100.85(16)
	δ-C	83.62(86)
	C=O	163.62(12)
		164.19(11)
		166.21(19)
		167.22
	OMe	50.95
		51.36
		52.55
		52.87

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; [$^2H_8$]Toluene, -70 °C.

[b] Major rotamer.

[c] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^2H]Chloroform, 26 °C.

acetylenedicarboxylate can be trapped, if sulphur is present, to give the thiocarbonyl compound (34)[15] [see Introduction].



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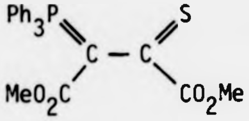
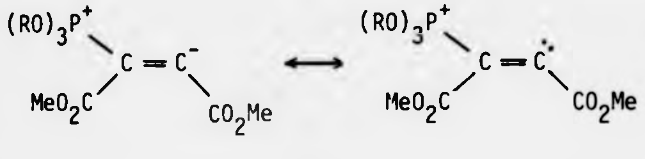
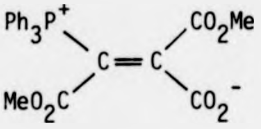


(34)



(87)



(31)

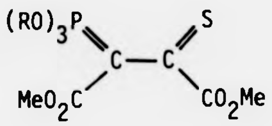
Since it has been suggested that this behaviour is indicative of the nucleophilic carbene character of the 1:1 intermediate (29)[15], it was of interest to see if the corresponding intermediate (87; R = alkyl) would show similar characteristics. We have therefore investigated the possibility of using elemental sulphur to trap the 1:1 intermediate initially formed in the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate. However, since the trialkyl phosphites showed a tendency to react preferentially with the sulphur to give the corresponding thiophosphate rather than with the dimethyl acetylenedicarboxylate, it proved to be difficult to generate the 1:1 intermediate (87; R = alkyl) in the presence of sulphur. This problem had been less marked in the reactions involving triphenylphosphine. Furthermore, in the case of the reaction involving triphenylphosphine it had been possible to generate the 1:1 intermediate (29) by the decomposition of the "CO_2-adduct" (31).[15] It had thus been possible to prepare and hence characterise the thiocarbonyl compound (34) by reacting the regenerated 1:1 adduct

(29) with sulphur in the absence of free phosphine. This approach could not be used to provide a convenient source of the intermediate (87; R = alkyl).

The reactions of trimethyl and triethyl phosphite with dimethyl acetylenedicarboxylate in the presence of sulphur were therefore investigated under a variety of conditions. At low sulphur levels trapping was relatively ineffective while increasing the amount of sulphur present to improve the trapping efficiency tended to suppress the formation of the 1:1 intermediate (87; R = Me, Et) and increase the degree of thiophosphate formation. The nature of the reaction solvent and the rate of mixing of the reactants were also found to be very important.

Fortunately, after numerous attempts, conditions were obtained which led to the formation of significant quantities of the desired thiocarbonyl compound (103; R = Et) at $\delta(^{31}P)$ 37.48 p.p.m. This was achieved using equimolar quantities of triethyl phosphite, the acetylene and sulphur with benzene as the solvent [see Experimental Section].

The presence of the thiocarbonyl group in (103; R = Et) was readily confirmed by the ^{13}C n.m.r. spectrum (Table 14) which clearly showed a characteristically low field resonance at δ_C 207.4 p.p.m. ($^2J_{PC}$ 13 Hz). The ylidic α-carbon was also clearly visible in the ^{13}C n.m.r. spectrum at δ_C 93.3 p.p.m. with an associated characteristic large $^1J_{PC}$ coupling of 206 Hz.

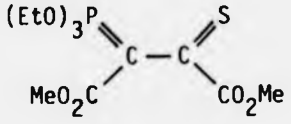


(103)

TABLE 14

^{13}C N.m.r. spectral data

1,2-Bis(methoxycarbonyl)-2-thioxoethylidenetriethoxyphosphorane (103).

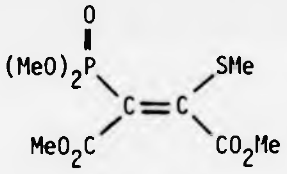


(103)

	δ^a
Et	12.06
	61.20
OMe	49.30
α-C	93.27(206)
C=O	165.20
C=S	207.4(13)

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

An interesting phenomenon was observed when the preparation of the thiocarbonyl compound (103; R = Me) was attempted using trimethyl phosphite. As expected the reaction of trimethyl phosphite with dimethyl acetylenedicarboxylate in the presence of sulphur, under similar conditions to those used for the preparation of (103; R = Et), also led to the formation of the thiocarbonyl compound (103; R = Me) at $\delta(^{31}P)$ (C_6D_6) 45.3 p.p.m. However, this thiocarbonyl (103; R = Me) was less stable than its ethyl analogue (103; R = Et) and slowly converted to the phosphonate (104) at $\delta(^{31}P)$ 15.1 p.p.m. over 4 h. at room temperature.



(104)

The same effect was also produced more rapidly when attempts were made to purify the thiocarbonyl compound (103; R = Me) by preparative thin layer chromatography on silica gel. A pure sample of this rearrangement product was thus obtained by preparative thin layer chromatography and confirmed as the phosphonate (104). The structure of the phosphonate (104) is consistent with the ^{31}P n.m.r. chemical shift which showed a marked upfield shift relative to the phosphorane (103; R = Me). Furthermore, the multiplicity of the proton-coupled ^{31}P n.m.r. signal clearly indicated that one of the methoxy groups on the phosphorus had been lost. In addition, the loss of the thiocarbonyl group and the formation of an S-methyl group during the rearrangement was clearly shown by the ^{13}C n.m.r. spectrum of the phosphonate (104; R = Me) (Table 15) with a methyl resonance at

δ_C 15.75 p.p.m. and the absence of a resonance signal for the thiocarbonyl group. The non-protonated α- and β-carbons were also readily identified in the ^{13}C n.m.r. spectrum by their couplings to phosphorus. These signals collapsed to singlets when the phosphorus signal at δ_P 15.1 p.p.m. was irradiated.

It is envisaged that the rearrangement of the initially formed thiocarbonyl compound (103; R = Me) is favoured due to the formation of the more stable phosphonate grouping of (104). The dealkylation of the phosphonium centre can be rationalised as a consequence of the formation of the 1,4-zwitterionic structure (105), as shown in Fig. 23, although an intermolecular dealkylation mechanism cannot be ruled out.

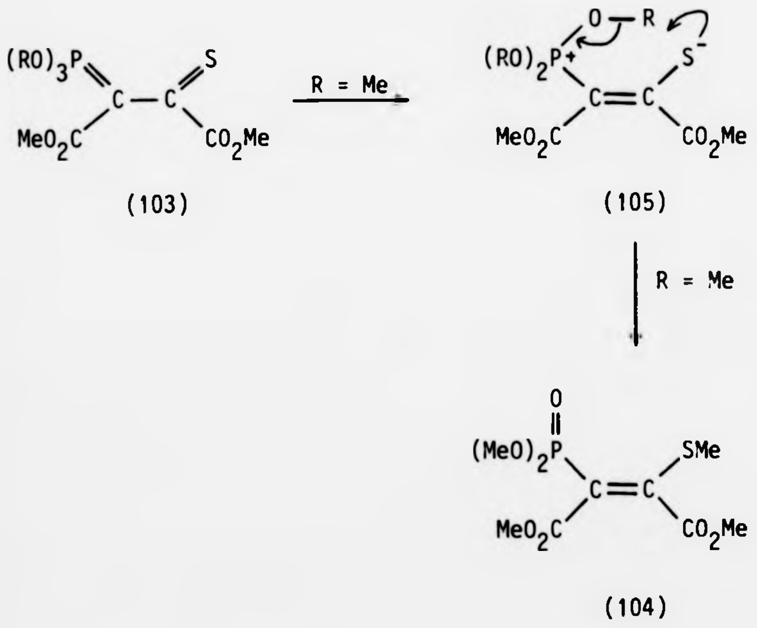


Fig. 23

TABLE 15

^{13}C N.m.r. spectral data

Dialkyl 2-alkylthio-1,2-bis(methoxycarbonyl)thioethylidenephosphonate (104 and 106).

δ[a]	(104) R = Me	(106) R = Et	
SR	15.75	13.59[b]	13.39[c]
		27.17	27.08
OMe	52.64	52.42	52.18
	52.74	52.68	52.86
P-OR	53.09(6)	16.19(6)	16.12(6)
		62.63(6)	62.52(5)
α-C	113.81(189)	115.77(186)	114.47(182)
β-C	165.77(7)	d	e
α-C=O	163.84(21)	d	e
β-C=O	163.59	d	e

[a] Shifts in p.p.m. from Me$_4$Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

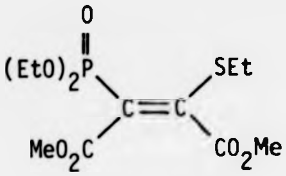
[b] Major rotamer.

[c] Minor rotamer.

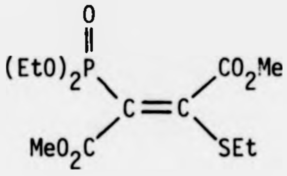
[d] 163.1 - 164.5, complex grouping (β-C, α-C=O and β-C=O).

[e] 163.1 - 164.9, complex groupling (β-C, α-C=O and β-C=O).

Interestingly a similar rearrangement was observed when attempts were made to purify the thiocarbonyl compound (103; R = Et) by chromatography on silica. However, in this latter case a mixture of both the *cis* and *trans* isomers of the phosphonate (106a and 106b) were produced (Table 15).



(106a)



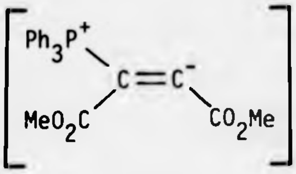
(106b)

We have also shown that it is possible to bring about the rearrangement of the thiocarbonyl compound (103; R = Et) to the phosphonate (106) by heating in benzene under reflux. The rearrangement had a half-life of about 5 h. under these conditions. Once again both isomers (106a) and (106b) were produced.

4. THE USE OF CARBON DIOXIDE TO TRAP THE 1:1 INTERMEDIATE FORMED IN THE REACTION OF DIMETHYL ACETYLENEDICARBOXYLATE WITH A VARIETY OF TRIVALENT PHOSPHORUS COMPOUNDS.

It has been previously reported that the 1:1 intermediate (29) formed from the reaction of triphenylphosphine with dimethyl acetylenedicarboxylate can be effectively trapped if carbon dioxide is bubbled through the reaction mixture while the intermediate is being generated.[2,21] The unstable adduct produced, a pale yellow solid, was assigned the structure (31) which may be considered as an internal salt of a half-ester of malonic acid [see Introduction].

The rapid reaction with carbon dioxide would suggest that here it is the anionic character of the 1:1 intermediate (29) rather than its carbene character which is important.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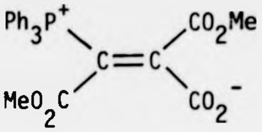
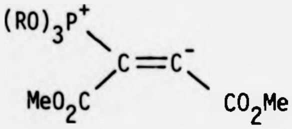

(31)

We have now studied the analogous reaction using trialkyl phosphites rather than triphenylphosphine. This work is discussed in considerable detail later in this thesis and therefore only a brief description of the relevant aspects of this reaction will be given at this point.

In essence, the reaction of the carbon dioxide with the 1:1 intermediates (87; R = alkyl) proceeds in a similar manner to that observed in the triphenylphosphine reaction. However, the high field ^{31}P n.m.r. resonance signal of the resulting product (e.g. δ_P - 50.9 p.p.m. for the CO_2-adduct from trimethyl phosphite) clearly indicated that the adduct was not the carboxylate betaine (107; R = Me), but the oxaphospholene (108; R = Me).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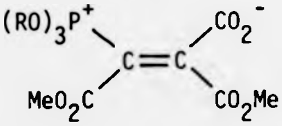
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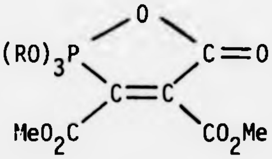

(108)

Nevertheless, we must still conclude that the reaction of carbon dioxide with the 1:1 intermediate (87; R = alkyl) proceeds via the anionic form of the intermediate rather than its carbenoid form.

5. SUMMARY

The evidence we have obtained from the reaction of tertiary phosphorus compounds with dimethyl acetylenedicarboxylate supports the view that the reactions pass through a 1:1 intermediate [see Introduction]. The nature of this 1:1 intermediate (1) is however less clear. There is some evidence that it can exhibit nucleophilic carbene character as, for example, in its reaction with sulphur [see earlier Discussion] and in the formation of the 1,2-diphosphoranes (88) and (90), [see Introduction and earlier Discussion]. However, these reactions can also be explained by anionic mechanisms, and an anionic mechanism is certainly followed in the reaction of the 1:1 intermediates (29) and (87) with carbon dioxide [see earlier Discussion].

The most effective way of demonstrating the presence of a carbene is by the addition of materials to the reaction mixture to trap the carbene intermediate once formed. However, as the reactants in the formation of the 1:1 intermediates are themselves efficient carbene traps this posed additional problems. The failure of attempts to use carbene traps such as cyclohexene to trap the 1:1 intermediate was therefore not unexpected. For this reason attempts were made to use an intramolecular carbene trap. Diallyl acetylenedicarboxylate (109)[71] was therefore prepared and its reaction with trimethyl phosphite investigated in the hope that the 1:1 intermediate formed with dimethyl acetylenedicarboxylate might undergo intramolecular carbene insertion (Fig. 24).

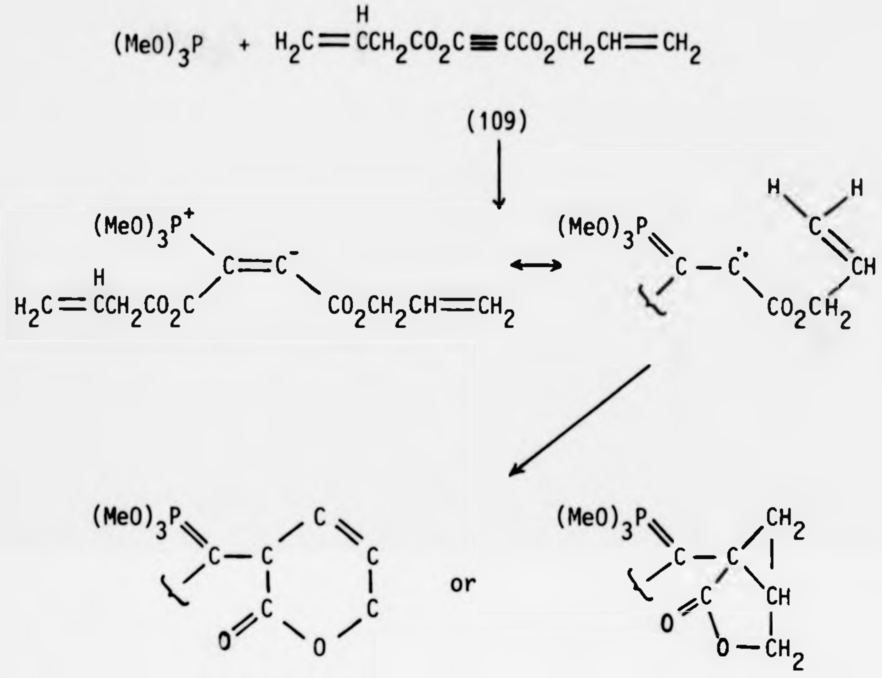
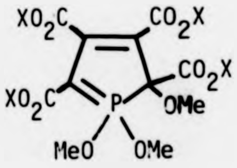


Fig. 24

However, the use of diallyl acetylenedicarboxylate, rather than dimethyl acetylenedicarboxylate in the reaction with trimethyl phosphite did not appear to interfere with the normal course of reaction and led to the formation of the cyclic ylide (110; $X = -CH_2CH{=}CH_2$). No intramolecular carbene insertion product was observed.



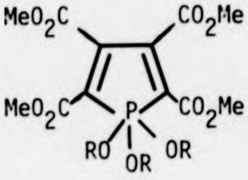
(110)

CHAPTER 2

Oxo-phospholes from Trivalent Phosphorus Compounds and Dimethyl Acetylenedicarboxylate.

1. PREPARATION OF OXO-PHOSPHOLES FROM n^5-PHOSPHOLES

We have already discussed the formation of the n^5-phospholes (95; R = alkyl) and (98; R' = aryl and alkyl) by the reaction of trialkyl phosphites or dialkyl phosphonites with dimethyl acetylenedicarboxylate at low temperatures. We have now investigated further the observation that treatment of the n^5-phospholes (95; R = alkyl), from the trialkyl phosphite reactions, with anhydrous hydrogen bromide causes the formation of the novel oxo-phospholes (111; R = alkyl). In particular we have investigated the possibility of improving the procedures for treating the unstable n^5-phospholes (95; R = alkyl) with hydrogen bromide in order to increase the yields of the oxo-phospholes (111; R = alkyl) from the modest yields originally reported. We have also investigated the possibility of preparing the oxo-phospholes (112; R' = aryl, alkyl) by treating the n^5-phospholes (98; R' = aryl, alkyl) with hydrogen bromide. However, we were aware, from our studies of the formation of the n^5-phospholes (98; R' = phenyl and methyl), that it would be considerably more difficult to trap these intermediates by reaction with hydrogen bromide because of their reduced thermal stability relative to the n^5-phospholes (95; R = alkyl) formed in the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate.



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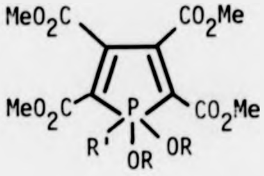

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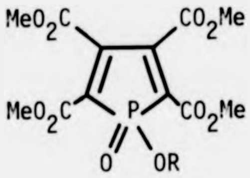

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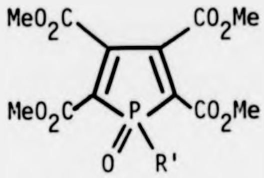


(112)

1.1. Oxo-phospholes from 1,1,1-trialkoxy-n^5-phospholes.

Shortly before commencing our study it had been shown by Griffiths and Tebby[50] that bubbling anhydrous hydrogen bromide into a solution of the n^5-phosphole (95; R = Me) in toluene caused the formation of the oxo-phosphole (111; R = Me) (see Fig. 25).

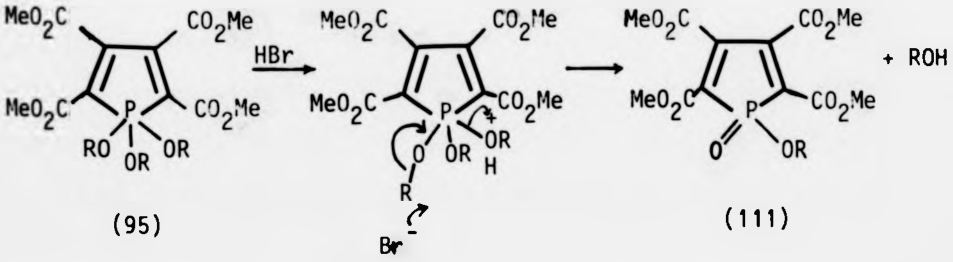


Fig. 25

However, this procedure was not particularly convenient to carry out in practice since it required access to an n.m.r. spectrometer to monitor the course of the reaction. Since the hydrogen bromide bubbled through the toluene solution without dissolving to any appreciable extent it was difficult to assess how much hydrogen bromide had been added and thus if the reaction was complete. A colour change from red-orange to yellow-green was observed as the reaction proceeded but it was easy to treat the n^5-phospholes (95; R = alkyl) with too much hydrogen bromide. Furthermore, addition of an excess of hydrogen bromide to the n^5-phospholes (95; R = alkyl) had been shown to lead to dealkylation of the initially-formed oxo-phosphole (111; R = alkyl) to give the "hydroxy-system"[50] (111; R = H).

To overcome these problems we have investigated the use of other solvents for the reaction. Since hydrogen bromide dissolves readily in diethyl ether it was felt that this solvent might allow a greater control of the amount of hydrogen bromide added to the solution of the n^5-phospholes. Although in general this belief was confirmed, in practice there was a drawback in that the use of diethyl ether rather than toluene as the reaction solvent led to the formation of slightly less pure samples of the n^5-phospholes (95; R = alkyl). Nevertheless, the use of diethyl ether did increase the overall yields of the oxo-phospholes (111; R = alkyl).

Two methods were devised for adding the hydrogen bromide to the n^5-phospholes (95; R = alkyl) in ether which gave a high conversion to the desired oxo-phospholes (111; R = alkyl). In the first method a known weight of hydrogen bromide was dissolved in a known volume of diethyl ether. An appropriate quantity of the solution was then cooled to about -10 °C and added to the solution of the n^5-phosphole (95; R = alkyl) in diethyl ether also at low temperature.

In the second method, a solution of the n^5-phosphole (95; R = alkyl) in ether at about -50 °C was transferred to a thermally insulated dropping funnel and added dropwise to the appropriate volume of gaseous hydrogen bromide cooled to about 0 °C. In this latter method the oxo-phosphole (111; R = Et) was formed as a white crystalline solid which was thrown onto the walls of the flask as a result of the vigorous nature of the reaction between the n^5-phosphole (95; R = Et) and the hydrogen bromide. An additional crop of the oxo-phosphole was also obtained by removing the ether and other volatile components from the solution left in the flask at the end of the reaction.

The only disadvantage of the method using gaseous hydrogen bromide was that it involved the additional complication of ensuring that the temperature of the solution of the n^5-phosphole (95; R = alkyl) did not rise above about -20 °C. However, providing that the solution of the n^5-phosphole was cooled to about -50 °C before being transferred to the dropping funnel and provided also that the dropping funnel was well insulated, this was not usually found to be a major problem.

Both improved methods returned similar yields for the preparation of the oxo-phosphole (111; R = Et) (54 and 59% respectively) which were much better than those previously reported (25-30%). In the case of the oxo-phosphole (111; R = Me), however, the improvement in yield was less marked due largely to the difficulties experiences in isolating the product.

The oxo-phospholes (111; R = alkyl) were readily identified by their chemical shift and the multiplicities of their resonances in the proton-coupled ^{31}P n.m.r. spectra (see Table 16). In particular the multiplicity of the resonance clearly indicated that only one alkyoxy group remained attached to the phosphorus atom. The ^{13}C n.m.r. spectrum, on the other hand, demonstrated clearly the symmetrical nature of the oxo-phospholes (111; R = alkyl). Thus, for example, the four heterocyclic ring carbons gave rise to only two doublets, one for the two *α*-carbons and one for the two *β*-carbons (see Table 16 and Plate 8) for ^{13}C n.m.r. spectrum of (111; R = Me).

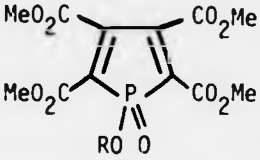
1.2 Oxo-phospholes from 1,1-dialkoxy-1-aryl-η^5-phospholes.

Attempts to prepare the oxo-phospholes (112; R' = alkyl, aryl) in an analogous way using dialkyl alkylphosphonites and dialkyl arylphosphonites in the place of trialkyl phosphites were generally less successful, as anticipated, due largely to the reduced stability of the η^5-phospholes (98; R = alkyl, R' = aryl, alkyl) over those derived from the trialkyl phosphites, (95; R = alkyl). However, by generating the η^5-phosphole (98; R = Et, R' = Ph) at -70 °C in toluene and treating it at this temperature with hydrogen bromide it was possible to obtain the oxo-phosphole (112; R' = Ph). Indeed, the ^{31}P n.m.r. spectrum of the reaction mixture following the treatment with hydrogen bromide showed the desired oxo-phosphole (112; R' = Ph) in about 40% yield. In this particular reaction there was no advantage in attempting to use the improved trapping methods which had proved so successful for the formation of the oxo-phospholes (111; R= alkyl). In the case of the η^5-phospholes (98; R = alkyl, R' = Ph) and (98; R,R' = alkyl) the thermal instability of these phospholes was the primary concern. The use of toluene as the reaction solvent and the necessity of maintaining the very low temperatures needed to avoid rearrangement took priority

TABLE 16

N.m.r. spectral data.

Tetramethyl 1-Alkoxy-1-oxo-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (111).



		R=Me	R=Et	R=Pr^i
δ(^{31}P)[a]		36.88	35.28	33.96[b]
		(q, 12)	(t, 9)	(d, 9)
δ(^{13}C)[c]				
	α-C	127.06(125)	127.55(125)	127.91(125)
	β-C	244.28(27)	144.03(28)	143.88(28)
	C=O	160.27(12)	160.16(12)	160.30(12)
		162.14(13)	162.20(23)	162.43(23)
	OMe	53.20	53.13	53.04
		53.30	53.25	53.28
	R	53.94(7)	16.49(6)	24.04(4)
			64.35(7)	74.21(7)

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; J_{PH} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] δ_P 32.43 p.p.m. [$^2H_8$]Toluene, 26 °C.

[c] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

^{13}C N.m.r. spectrum of tetramethyl 1-methoxy-1-oxo-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (111; R = Me) (proton decoupled).

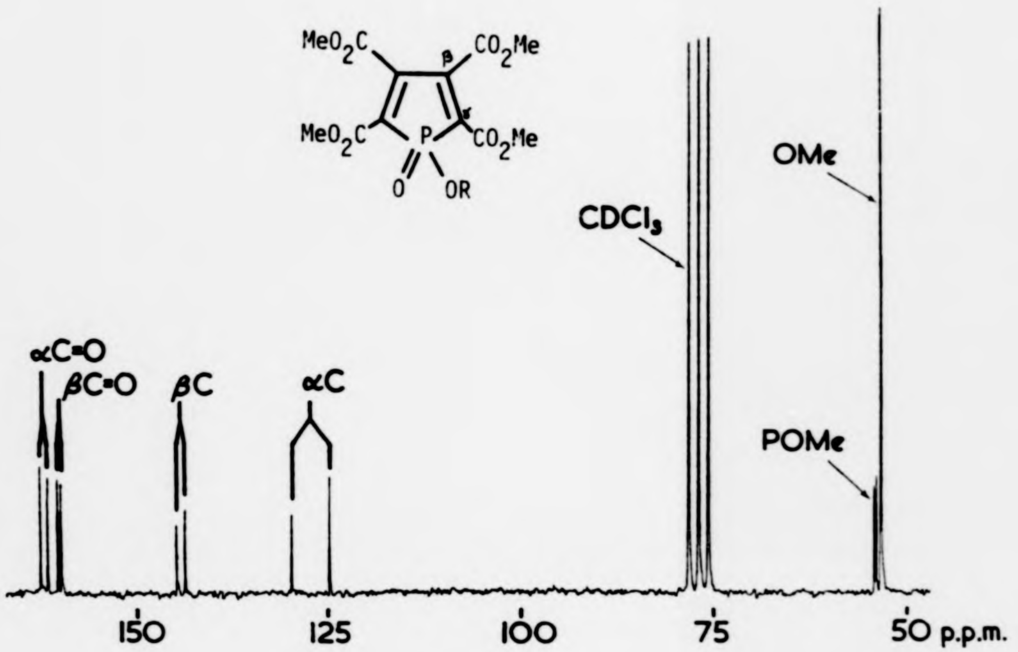
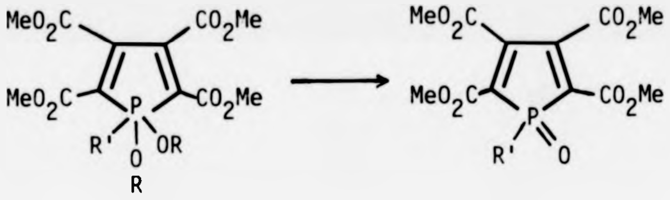


Plate 8

over the convenience of adding the hydrogen bromide to an ethereal solution of the η^5-phosphole (98). A modest quantity of the oxo-phosphole (112; R' = Ph) was isolated in a pure state from the reaction mixture in the usual manner and gave ^{31}P and ^{13}C n.m.r. spectra (Table 17) consistent with the proposed spectra. Moreover, both the η^5-phospholes (98; R = Me, R' = Ph) and (98; R = Et, R' = Ph) gave the same product on treatment with hydrogen bromide, confirming the loss of the alkoxy groups, originally on the phosphorus, from the molecule.



(98) R=Me, Et, R'=Ph (112) R'=Ph

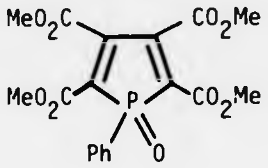
The proton-coupled ^{31}P n.m.r. spectrum of the oxo-phosphole (112; R' = Ph) showed a triplet ($^3J_{PH}$ 14 Hz) at δ_P 38.7 p.p.m. due to coupling with the ortho protons on the phenyl ring. The ^{13}C n.m.r. spectrum showed the symmetrical nature of the molecule in that only two doublets were observed for the four carbon atoms of the heterocyclic ring (Table 17) (Plate 9).

Interestingly, attempts to isolate further quantities of the oxo-phosphole (112; R' = Ph) from the reaction mixture were less successful. Although the crude phosphole did gradually crystallise on standing to give a pure compound this material

TABLE 17

N.m.r. spectral data.

Tetramethyl 1-Oxo-1-phenyl-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (112)



$\delta(^{31}P)^a$		38.7 (t, 14)
$\delta(^{13}C)^b$		
	α-C	132.58(88)
	β-C	145.76(20)
	C=O	160.29(12)
		162.07(18)
	OMe	53.08
		53.35
	Ar	123.33(107)
		129.14(13)
		130.30(12)
		133.73(3)

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; [^{2}H]Chloroform, 26 °C.

[b] Shifts in p.p.m. from Me$_4$Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

^{13}C N.m.r. spectrum of tetramethyl 1-oxo-1-phenyl-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (112; R' = Ph) (proton decoupled).

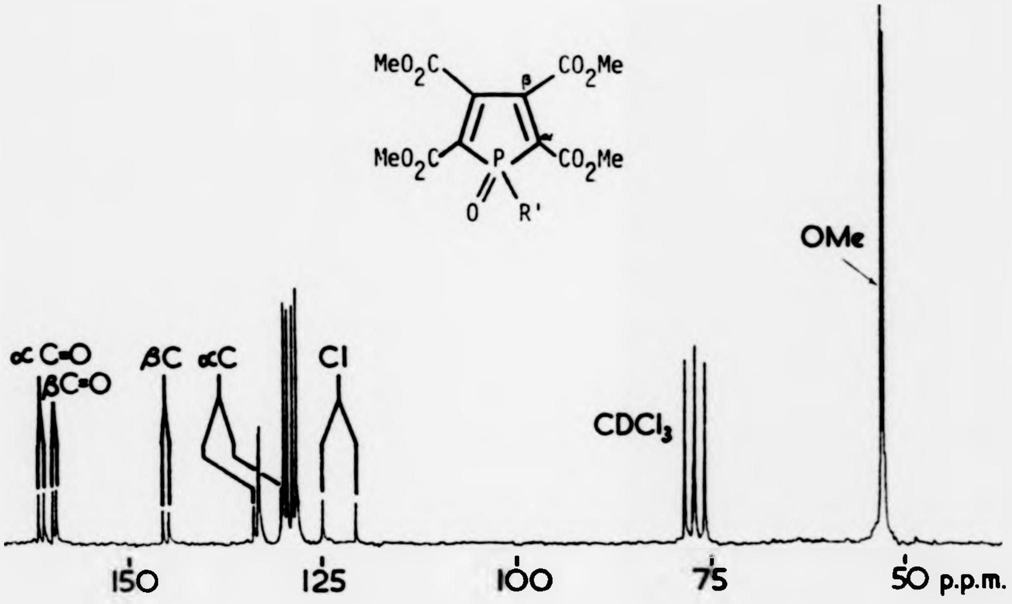
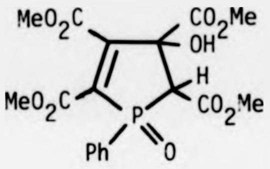


Plate 9

was not the expected oxo-phosphole (112; R' = Ph) but the hydrated system, the oxo-phospholene (113). This same oxo-phospholene (113) was also obtained when attempts were made to isolate a pure sample of the oxo-phosphole (112; R' = Ph) from another sample of the crude material by chromatography on silica. The oxo-phospholene (113) was readily identified by its combustion analysis its ^{31}P and ^{13}C n.m.r. spectra (Table 18) (Plate 10), and other spectroscopic data [see Experimental Section].



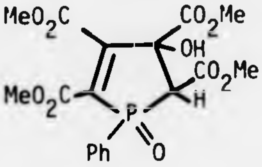
(113)

Thus, for example the ^{13}C n.m.r. spectrum of the "hydrated" phosphole, oxo-phospholene (113) (Table 18), clearly showed that the symmetrical nature of the heterocyclic ring had been lost since the four ring carbons were now observed as four discrete doublets. Furthermore, two of these doublets, those at $\delta(^{13}C)$ 59.83 and 79.05 p.p.m., were clearly no longer from sp^2 hybridised carbon atoms. Since the J_{PC} coupling to the signal at $\delta(^{13}C)$ 59.83 p.p.m. was 59 Hz and that to the signal at $\delta(^{13}C)$ 79.05 p.p.m. was only 15 Hz it was also clear that only one of these carbons, that at δ_C 59.83 p.p.m., was adjacent to the phosphorus atom. This clearly indicated that the hydration product was an oxo-2-phospholene (114), rather than an oxo-3--phospholene (115).

TABLE 18

N.m.r. spectral data.

Tetramethyl 5-Hydro-4-hydroxy-1-oxo-1-phenyl-2-phospholene-2,3,4,5-tetracarboxylate (113).



(113)

δ(^{31}P)^a		
		43.44 (d of t; 28, 15)
δ(^{13}C)^b		
	α-C	133.02(84)
	β-C	156.50(16)
	γ-C	79.05(15)^c
	δ-C	59.83(59)^d
	C=O	161.45(9)
		162.68(19)
		164.99
		169.41
	OMe	52.55
		53.20
		53.20
		53.64

TABLE 18 continued

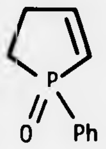
Ar	126.49(110)
	127.97(13)
	131.84(11)
	133.19(3)

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; J_{PC} in Hz in parentheses.

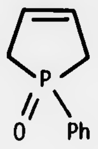
[b] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[c] ^{13}C n.m.r. proton-coupled spectrum: $^2J_{CH}$ 7 Hz, d.

[d] ^{13}C n.m.r. proton-coupled spectrum: $^1J_{CH}$ 129 Hz, d.



(114)



(115)

Since the proton-coupled ^{13}C n.m.r. spectrum of the oxo-phospholene showed that the signal at δ_C 59.83 p.p.m. was a doublet ($^1J_{CH}$ 129 Hz) and thus protonated, the orientation of addition of the water across the oxo-phosphole (112; R' = Ph) was clearly as indicated in the phospholene (113). This is also consistent with that predicted from a consideration of the mechanism of hydration.

It is interesting to note the apparently increased susceptibility of the oxo-phosphole (112; R' = Ph) to nucleophilic attack relative to the alkoxy substituted oxo-phospholes (111; R = alkyl) previously prepared. As expected the pure sample of the oxo-phosphole (112; R' = Ph) which had been initially isolated also became hydrated to give the oxo-phospholene (113) on exposure to the atmosphere.

Attempts to reverse the hydration by acid or base catalysed dehydration using a variety of methods were unsuccessful.

1.3 Oxo-phospholes from 1,1-dialkoxy-1-alkyl-n^5-phospholes.

The still further reduced thermal stability of the intermediates formed in the reaction of dimethyl methylphosphonite with dimethyl acetylenedicarboxylate, as previously mentioned [see earlier Discussion], prevented the formation of the desired n^5-phosphole

^{13}C N.m.r. spectrum of tetramethyl 5-hydro-4-hydroxy-1-oxo-1-phenyl-2-phospholene-2,3,4,5--tetracarboxylate (113) (proton decoupled).

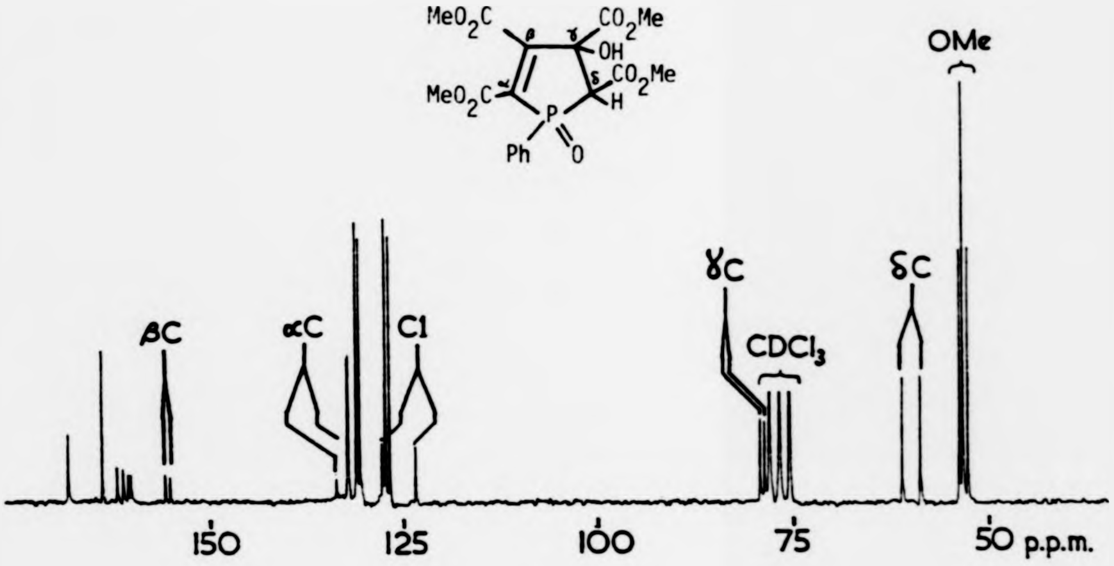
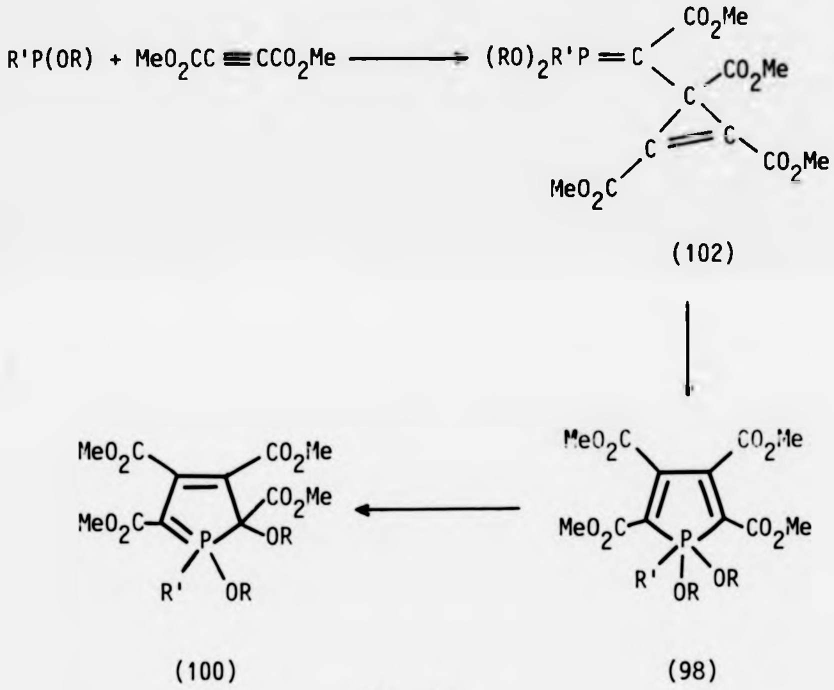


Plate 10

precursor (98; R, R' = Me) in high yield. The conditions needed to facilitate the formation of the n^5-phosphole (98; R, R' = Me) from its ylide precursor (102; R, R' = Me) also led to the rearrangement of the n^5-phosphole (98; R, R' = Me) to the cyclic ylide (100; R, R' = Me), (see Fig. 26).



(102)

(100)

(98)

Fig. 26

Despite considerable efforts it was difficult to obtain a ^{31}P n.m.r. signal for the n^5-phosphole (98; R, R' = Me) greater than about 20% of the total ^{31}P n.m.r. signal for the reaction mixture. Although this was not sufficiently high to enable the oxo-phosphole (112; R' = Me) to be produced on a preparative basis we were able to show by ^{31}P n.m.r. spectroscopy that treatment of the n^5-phosphole (98; R, R' = Me) with anhydrous hydrogen bromide did give the oxo-phosphole (112; R' = Me) [δ_P 46.1 p.p.m., q, $^2J_{PH}$ 15 Hz].

precursor (98; R, R' = Me) in high yield. The conditions needed to facilitate the formation of the n^5-phosphole (98; R, R' = Me) from its ylide precursor (102; R, R' = Me) also led to the rearrangement of the n^5-phosphole (98; R, R' = Me) to the cyclic ylide (100; R, R' = Me), (see Fig. 26).

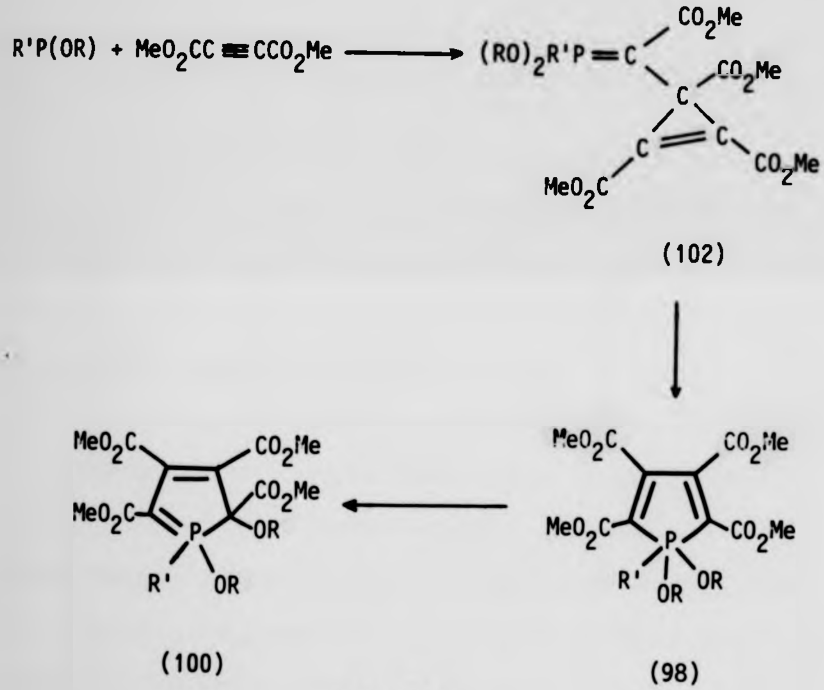


Fig. 26

Despite considerable efforts it was difficult to obtain a ^{31}P n.m.r. signal for the n^5-phosphole (98; R, R' = Me) greater than about 20% of the total ^{31}P n.m.r. signal for the reaction mixture. Although this was not sufficiently high to enable the oxo-phosphole (112; R' = Me) to be produced on a preparative basis we were able to show by ^{31}P n.m.r. spectroscopy that treatment of the n^5-phosphole (98; R, R' = Me) with anhydrous hydrogen bromide did give the oxo-phosphole (112; R' = Me) [δ_P 46.1 p.p.m., q, $^2J_{PH}$ 15 Hz].

precursor (98; R, R' = Me) in high yield. The conditions needed to facilitate the formation of the n^5-phosphole (98; R, R' = Me) from its ylide precursor (102; R, R' = Me) also led to the rearrangement of the n^5-phosphole (98; R, R' = Me) to the cyclic ylide (100; R, R' = Me), (see Fig. 26).

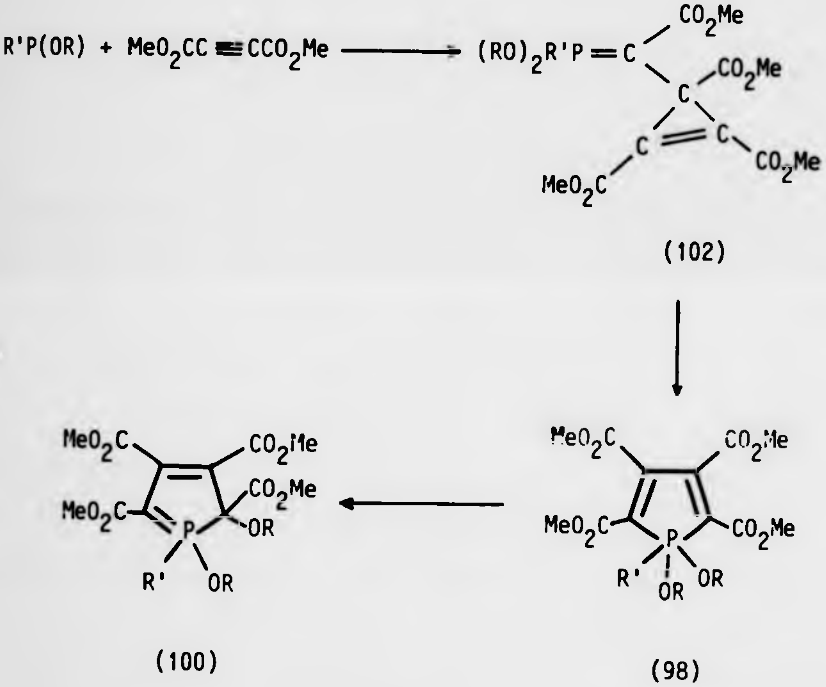
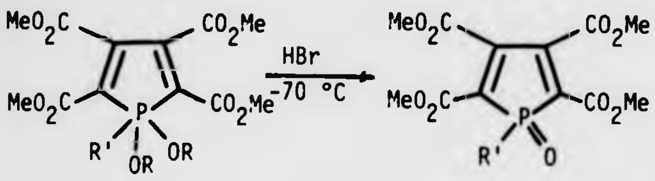


Fig. 26

Despite considerable efforts it was difficult to obtain a ^{31}P n.m.r. signal for the n^5-phosphole (98; R, R' = Me) greater than about 20% of the total ^{31}P n.m.r. signal for the reaction mixture. Although this was not sufficiently high to enable the oxo-phosphole (112; R' = Me) to be produced on a preparative basis we were able to show by ^{31}P n.m.r. spectroscopy that treatment of the n^5-phosphole (98; R, R' = Me) with anhydrous hydrogen bromide did give the oxo-phosphole (112; R' = Me) [δ_P 46.1 p.p.m., q, $^2J_{PH}$ 15 Hz].



(98) (112)

2. PREPARATION OF OXO-PHOSPHOLES FROM 2H-1λ^5-PHOSPHOLES

In view of the difficulties experienced in the preparation of those oxo-phospholes (112; R' = alkyl, aryl) possessing an alkyl or aryl substituent on the phosphorus, by the low temperature trapping route previously described, we have also looked for alternative methods for producing these oxo-phospholes.

Since rearrangement of the n^5-phospholes (98; R = alkyl, R' = phenyl or alkyl) led to the formation of the cyclic ylides (100; R = alkyl, R' = phenyl or alkyl) in which the alkyl and aryl group remained attached to the phosphorus atom [see previous Discussion], these cyclic ylides were considered to see if they might be suitable precursors for oxo-phospholes of the type (112; R' = alkyl, aryl).

It was noted that if the cyclic ylides (91; R = alkyl) or (100; R = alkyl, R' = aryl, alkyl) were treated with hydrogen bromide we would expect them to protonate and, the resulting quasi-phosphonium salts to subsequently dealkylate to give the oxo-phospholenes (116; R = alkyl, R' = alkoxy, alkyl or aryl) Fig. 27. The elimination of a molecule of alcohol from these oxo-phospholenes (116) would then in theory, lead to the formation of the desired oxo-phospholes (111) and (112).

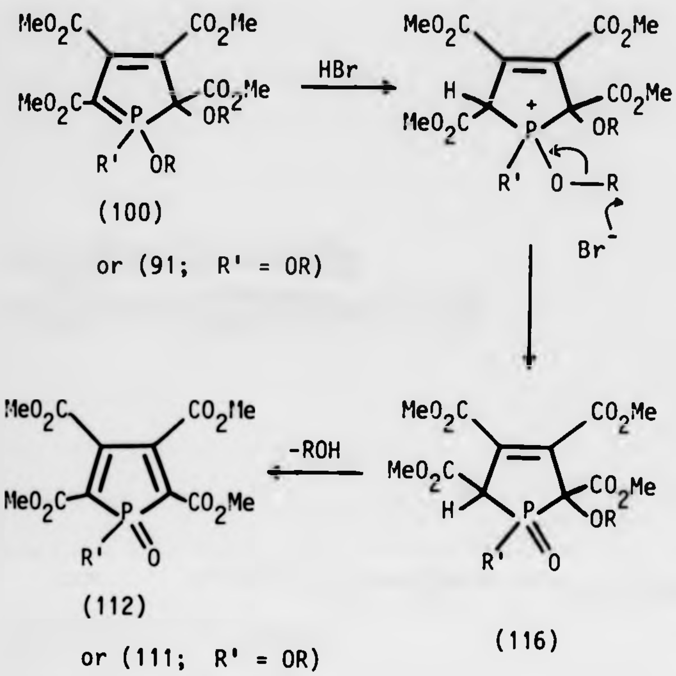


Fig. 27

To investigate this theory initial work was carried out on the cyclic ylides (91; R = alkyl) prepared by the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate.

2.1 Oxo-phospholes (111) from 1,1,2-trialkoxy-2H-1λ^5-phospholes (91; R = alkyl).

Since the course of the reaction was to be monitored initially by ^{31}P n.m.r. spectroscopy, it was important to choose a substituent on the phosphorus which would give a readily interpretable signal in the proton-coupled spectrum of the reaction mixture. The initial study was therefore carried out on the cyclic ylide (91; R = Pr^i) prepared from triisopropyl phosphite. If protonation and dealkylation did occur on treating the cyclic ylide (91; R = Pr^i) with hydrogen bromide the resulting oxo-phospholene (116; R = Pr^i, R' = OPr^i) would be expected to give a characteristic doublet of doublets in the proton-coupled ^{31}P n.m.r. spectrum.

A pure sample of the cyclic ylide (91; R = Pr^i) in toluene was therefore prepared, cooled in an ice-bath, and treated cautiously with anhydrous hydrogen bromide. The hydrogen bromide was bubbled slowly through the solution of the cyclic ylide until the red-orange colouration had been discharged and a lime-yellow colouration remained. The ^{31}P n.m.r. spectrum of the resulting solution confirmed that the signal for the cyclic ylide (91; R = Pr^i) at δ_P 76.5 p.p.m. [$^2H_8$] toluene, was no longer present and that it had been replaced by a large signal at δ_P 44.8 p.p.m. together with a number of other smaller signals between δ_P 45.6 and 41.2 p.p.m. (Plate 11). The proton-coupled ^{31}P n.m.r. spectrum of this material (Plate 11) showed the major signal to be a doublet of doublets ($^2J_{PH}$ 16 and 8 Hz). The presence of the larger coupling was interpreted as confirming that protonation had occurred at the ylidic $\underline{\alpha}$-carbon of the cyclic ylide (91; R = Pr^i) while the presence of only one other coupling clearly indicated that only one isopropoxy group remained attached to the phosphorus.

^{31}P N.m.r. spectra of the diastereoisomers of oxo-phospholene (116; R = Pr^i, R' = OPr^i).

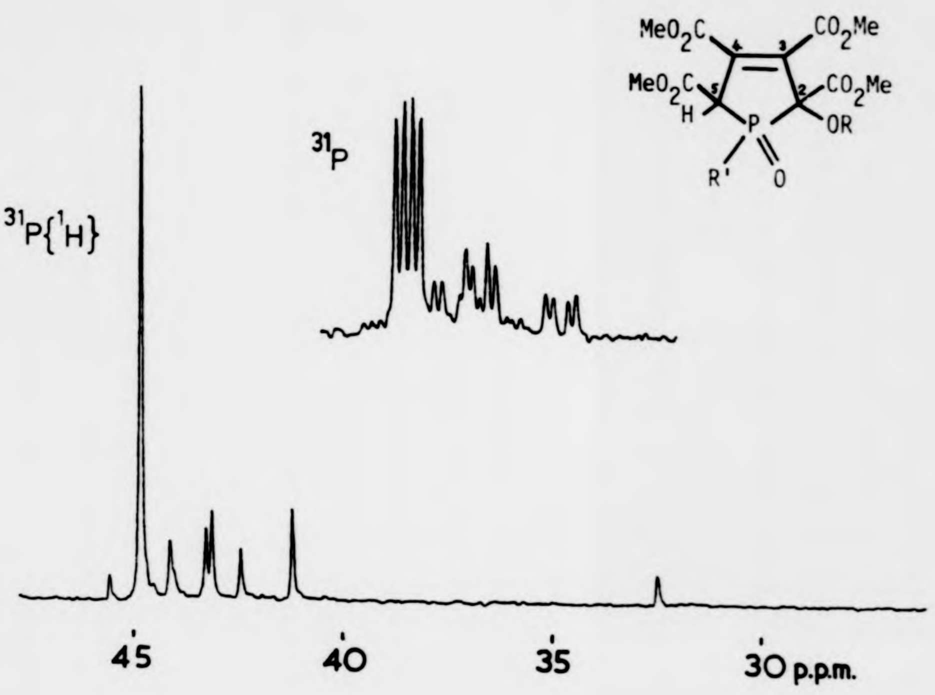


Plate 11

This in turn confirmed our earlier prediction that treatment of the cyclic ylides would not only result in protonation but also dealkylation of the resulting quasi-phosphonium salt. Most of the remaining small signals in the region of the large signal at $\delta(^{31}P)$ 44.8 p.p.m. were attributed to other diastereoisomers of the oxo-phospholene (116; R = Pr^i, R' = OPr^i). Over a period of time these minor signals became more intense at the expense of the major signal showing that equilibration of the diastereoisomers was occurring. The signals from these diastereoisomers also appeared as doublet of doublets although there were variations in the values of these couplings from those observed for the signal at $\delta(^{31}P)$ 44.8 p.p.m.

After a period of time a doublet began to appear in the proton-coupled ^{31}P n.m.r. spectrum of the reaction mixture at $\delta_P([^2H_8]$toluene) 32.4 p.p.m. ($^2J_{PH}$ 9 Hz) (Plate 12). This compound was readily identified as the desired oxo-phosphole (111; R = Pr^i) indicating that isopropanol was being spontaneously eliminated from the oxo-phospholene (116; R = Pr^i, R' = OPr^i). At room temperature the formation of the oxo-phosphole (111; R = Pr^i) was relatively slow but this process could be accelerated by heating the phospholene and placing it under reduced pressure. At a temperature of 50 °C and a pressure of 16 mm Hg the formation of the oxo-phosphole (111; R = Pr^i) was complete after 30 min. and, furthermore, ^{31}P n.m.r. spectroscopy indicated that no other phosphorus-containing compounds had been produced. Trituration of the resulting oil with diethyl ether caused the product to crystallise. The oxo-phosphole (111; R = Pr^i) was recovered in essentially quantitative yield. The ^{13}C and ^{31}P n.m.r. spectral data for the oxo-phosphole (111; R = Pr^i) are given in Table 16 (for ^1H n.m.r. spectral data see Experimental section).

^{31}P N.m.r. spectra of the oxo-phosphole (111; R = Pr^i) prepared from oxo-phospholene (116; R = Pr^i, R' = OPr^i).

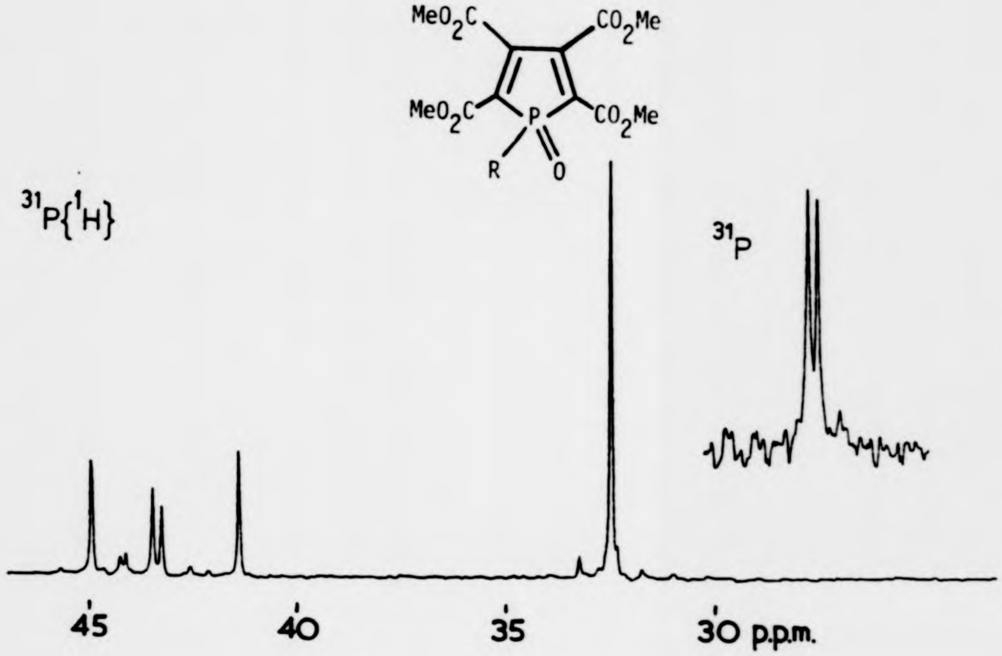


Plate 12

A similar procedure was used to prepare the analogous methoxy- and ethoxy-substituted oxo-phospholes (111; R = Me, Et) although in these cases the yields, although still good (∿60%) were lower than the excellent yield obtained for the isopropoxy-substituted oxo-phosphole (111; R = Pr^i).

The oxo-phospholes (111; R = alkyl) obtained in this way were identical to samples previously prepared by trapping the n^5-phosphole intermediates (95; R = alkyl) with hydrogen bromide at low temperatures as described earlier.

Interestingly, the rate of elimination of alcohol from the oxo-phospholene (116; R = alkyl, R' = alkoxy) was found to depend on the nature of the alkoxy group. Thus, after 17 h. at room temperature only a 25% conversion of the oxo-phospholene (116; R = Et, R' = OEt) to the oxo-phosphole (111; R = Et) had occurred, whereas in the case of the corresponding iso-propoxy system the conversion was about 50% after only 6 h. For the rate of conversion of the oxo-phospholene (116; R = Me, R' = OMe) to the oxo-phosphole (111; R = Me) see Experimental section. Nevertheless, in all cases studied the elimination of the molecule of alcohol from the oxo-phospholenes (116) had proved to occur much more readily than anticipated. For the ^{31}P n.m.r. spectral data of the oxo-phospholenes (116; R = alkyl, R' = alkoxy) see Table 19.

The route to the oxo-phospholes (111; R = alkyl) from the cyclic ylides (91; R = alkyl) thus proved to be superior to the method from the unstable n^5-phosphole (111; R = alkyl) which had been initially developed.

During the work to compare the samples of the oxo-phospholes (111; R = Pr^i) produced by the two different routes it was noted

TABLE 19

^{31}P N.m.r. spectral data.

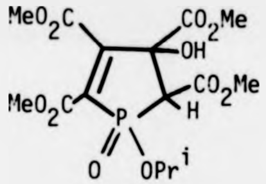
Tetramethyl 1,2-Dialkoxy-5-hydro-1-oxo-1-phenyl-3-phospholene--2,3,4,5-tetracarboxylate (116; R = alkyl, R' = OR).

R	δ[a]			
Et	48.46[b]	47.80	46.89[b]	45.58
Me	49.59[b]	49.23	48.76[b]	46.61

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; [^{2}H]Chloroform, 26 °C.

[b] Major isomers.

that some of the older samples of the oxo-phospholes had deteriorated. Indeed, in some cases no oxo-phosphole (111; R = Pr^i) remained. Instead the product was the "hydrated" system, the 2-phospholene (117). The ^{13}C n.m.r. spectrum of this system is shown in Table 20 and shows many of the features observed in the analogous phenyl system (113) previously discussed. Furthermore, the proton-coupled ^{31}P n.m.r. spectrum of the phospholene (117) was a doublet of doublets (J_{PH} 25 and 9 Hz), clearly indicating the presence of an additional proton coupling relative to that of the original oxo-phosphole (111; R = Pr^i).



(117)

No comparable behaviour was observed with samples of the methoxy- and ethoxy- oxo-phospholes (111; R = Me, and Et) even after exposure to the atmosphere for extended periods.

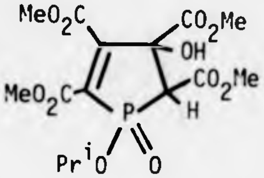
2.2 Oxo-phospholes (112) from 1,2-dialkoxy-1-aryl-2H-1λ^5-phospholes (100; R = alkyl, R' = aryl).

Having successfully demonstrated that it was possible to use the cyclic ylides (91) as precursors for the formation of the oxo-phospholes (111), we next turned our attention to the formation of the oxo-phospholes (112; R' = alkyl, aryl) which had proved difficult via the n^5-phosphole intermediates (98; R = alkyl, R' = aryl or alkyl).

TABLE 20

N.m.r. spectral data.

Tetramethyl 5-Hydro-4-hydroxy-1-oxo-1-phenyl-2-phospholene-2,3,4,5--tetracarboxylate (117).



$\delta(^{31}P)^{a,b}$		40.01 (d of d, 25,9)
$\delta(^{13}C)^{c,b}$		
	α-C	131.67(118)
	β-C	155.44(21)
	γ-C	77.14(5)
	δ-C	55.47(91)
	C=O	160.85(8)
		163.11(24)
		164.85(4)
		169.56
	OMe	52.82
		52.97
		53.09
		54.04
	Pr^i	23.89(4)
		73.02(7)

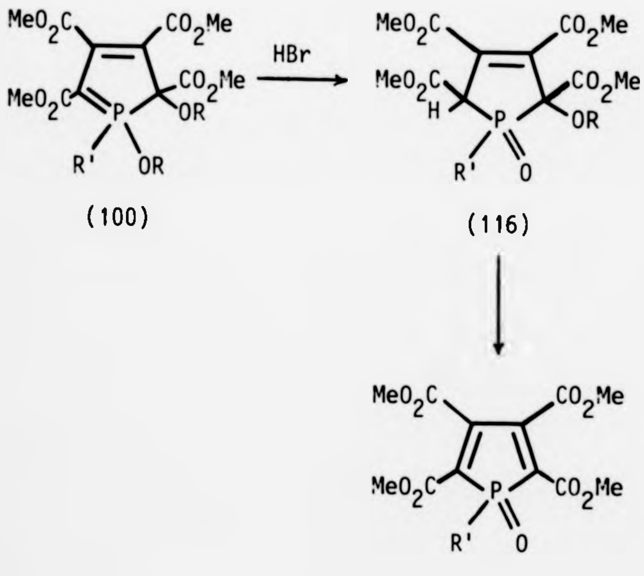
[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; multiplicity and J_{PH} in Hz in parentheses.

[b] [^{2}H]Chloroform, 26 °C.

[c] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses.

Since the dialkyl phenylphosphonites were most readily available the cyclic ylides (100; R = alkyl, R' = phenyl) derived from these compounds were the systems studied first.

The treatment of a solution of the cyclic ylide (100; R = alkyl, R' = phenyl) formed from either dimethyl or diethyl phenylphosphonite and dimethyl acetylenedicarboxylate with anhydrous hydrogen bromide in the usual way led to the formation of the phospholene (116; R = Me, Et, R' = phenyl). In this case, however, only two diastereoisomers of the phospholene were produced in significant quantities. For the phospholene (116; R = Me, R' = phenyl) the signals occurred at $\delta(^{31}P)$ 54.3 and 48.0 p.p.m. while those for the phospholene (116; R = Et, R' = phenyl) occurred at $\delta(^{31}P)$ 54.7 and 48.4 p.p.m.



(100)

(116)

(112)

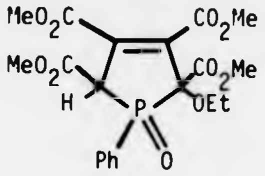
These phospholenes (116; R = Me, Et, R' = Ph) were considerably more stable than those which had been prepared from the cyclic ylides (116; R' = alkoxy, R = alkyl). In particular there was no significant elimination of alcohol from the phospholene (116; R = Et, R' = Ph) to give the oxo-phosphole (112; R' = Ph) at room temperature over a period of several hours. This meant that the phospholene (116; R = Et, R' = Ph) could be isolated in a pure form and analysed by n.m.r. spectroscopy and combustion analysis before it had rearranged [see Experimental section]. The predicted structure of the phospholene (116; R = Et, R' = Ph) was confirmed by ^{13}C n.m.r. spectroscopy (Table 21) which showed two distinct groups of signals for the two diastereoisomers. Fortunately, however, the phospholene (116; R = Et, R' = Ph) could be made to eliminate a molecule of ethanol to give the desired phenyl-substituted oxo-phosphole (112; R' = Ph) by heating it. However, at 60 °C and atmospheric pressure the conversion of the phospholene (116; R = Et, R' = Ph) to the oxo-phosphole (112; R' = Ph) was still relatively slow and only 30% complete after 5 h. Nevertheless, at 100 °C and under reduced pressure (16 mm Hg) the conversion could be accelerated and was complete within 1.5 h. It was later shown that over a period of several days the phospholene (116; R = Et, R' = Ph) was gradually converted to the oxo-phosphole (112; R' = Ph) even at room temperature and atmospheric pressure.

The oxo-phosphole (112; R' = Ph) produced from the cyclic ylide (116; R = Et, R' = Ph) was identical to that formed by treating the unstable n^5-phosphole intermediates (98; R = alkyl, R' = Ph) with anhydrous hydrogen bromide. For n.m.r. data see Table 17. Moreover, once again, considerable problems were encountered when trying to

TABLE 21

^{13}C N.m.r. spectral data.

Tetramethyl 2-Ethoxy-5-hydro-1-oxo-1-phenyl-3-phospholene-2,3,4,5--tetracarboxylate (116; R = Et, R' = Ph).



(116)

δ(^{13}C)[a]			
	α-C	89.38(69)	88.86(66)
	β-C	143.85(16)	143.25(15)
	γ-C	b	b
	δ-C	b	b
	C=O	164.63(3)	162.07(11)
		165.40	162.65(8)
		165.42(13)	162.96
		166.10(17)	163.38(5)
	OMe	c	c
	OEt	14.73	
		65.20(5)	64.99(6)
	Ar	124.34(93)	
		128.63(12)	
		132.02(9)	130.96(10)
		134.44(6)	132.32(6)

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [$^2H_8$]Toluene, 26 °C.

[b] Signal obscured.

[c] Multiple signals.

isolate the pure oxo-phosphole (112; R' = Ph). On every occasion some degree of hydration was found to have occurred to give some oxo-phospholene (113) as a contaminant. However, it is felt that rigorous exclusion of water from the work up procedure by use, for example, of a glove box could overcome these problems.

The oxo-phosphole (112; R' = Ph) was eventually isolated as the oxo-phospholene (113) in 87% yield, showing the obvious potential of this method for the preparation of other aryl-substituted oxo-phospholes of this type. As previously mentioned our attempts to "dehydrate" the oxo-phospholene (113) to give the oxo-phosphole (112; R' = Ph) were unsuccessful, although, there is some scope for further work here.

2.3 Oxo-phospholes from 1,2-dialkoxy-1-alkyl-2H-1λ^5-phospholes (100; R,R' = Me).

In view of our success with the preparation of the oxo-phospholes (112; R' = Ph) from the corresponding cyclic ylide (100; R = Me or Et, R' = Ph) we next investigated the preparation of the methyl-substituted system (112; R' = Me) which had proved to be inaccessible on a preparative scale via the low temperature trapping route previously discussed.

The treatment of the cyclic ylide (100; R,R' = Me) with anhydrous hydrogen bromide was carried out in the usual way and as anticipated the signal at $\delta(^{31}P)$ 97.4 p.p.m. corresponding to the cyclic ylide (100; R,R' = Me) was replaced by two signals at $\delta(^{31}P)$ 67.95 and 60.8 p.p.m. corresponding to two of the diastereoisomers of the phospholene (116; R,R' = Me). This oxo-phospholene (116; R,R' = Me) was heated at 50 °C under reduced pressure (16 mm Hg), until the elimination of methanol was complete (about 1 h), the only signal observable in the ^{31}P n.m.r. spectrum of the product at this time was that at δ_P 46.1 p.p.m. corresponding to the desired methyl substituted oxo-phosphole (112; R' = Me). As expected this signal was observed as a quartet ($^2J_{PH}$ 15 Hz) in the proton-coupled ^{31}P n.m.r. spectrum, confirming the presence of the methyl-substituent on the phosphorus. The proposed structure for the oxo-phosphole (112; R' = Me) was confirmed by the ^{13}C n.m.r. spectrum (see Table 22) (Plate 13). Interestingly, this oxo-phosphole (112; R' = Me) seemed less susceptible to hydration than the phenyl-substituted system (112; R' = Ph). There was, for example, no obvious signs of deterioration when samples of the solid oxo-phosphole (112; R' = Me) were left exposed to the atmosphere. It was also possible to chromatograph the oxo-phosphole (112; R' = Me) on silica using ethyl acetate as eluant. Although the losses on the chromatography plate were excessive a small quantity of the pure oxo-phosphole (112; R' = Me) was recovered from the chromatography plate.

3. ATTEMPTED REDUCTION OF OXO-PHOSPHOLES.

Since the oxo-phospholes (112; R' = alkyl, aryl) can in theory provide a route to the novel phospholes (118; R' = alkyl, aryl), attempts were made to reduce the phosphoryl group in (112; R' = Ph). The reagents normally employed for this purpose are the silyl hydrides,[58] with trichlorosilane ($HSiCl_3$) in benzene in the presence of a tertiary amine now being preferred to phenyl silane ($PhSiH_3$). However, it should be noted that such reductions have largely been restricted to phospholane oxides,[72,73] phospholene oxides[72] and a number of phosphole oxide dimers.[74] Nevertheless, trichlorosilane in

^{13}C N.m.r. spectrum of tetramethyl 1-methyl-1-oxo-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (112; R' = Me) (proton decoupled).

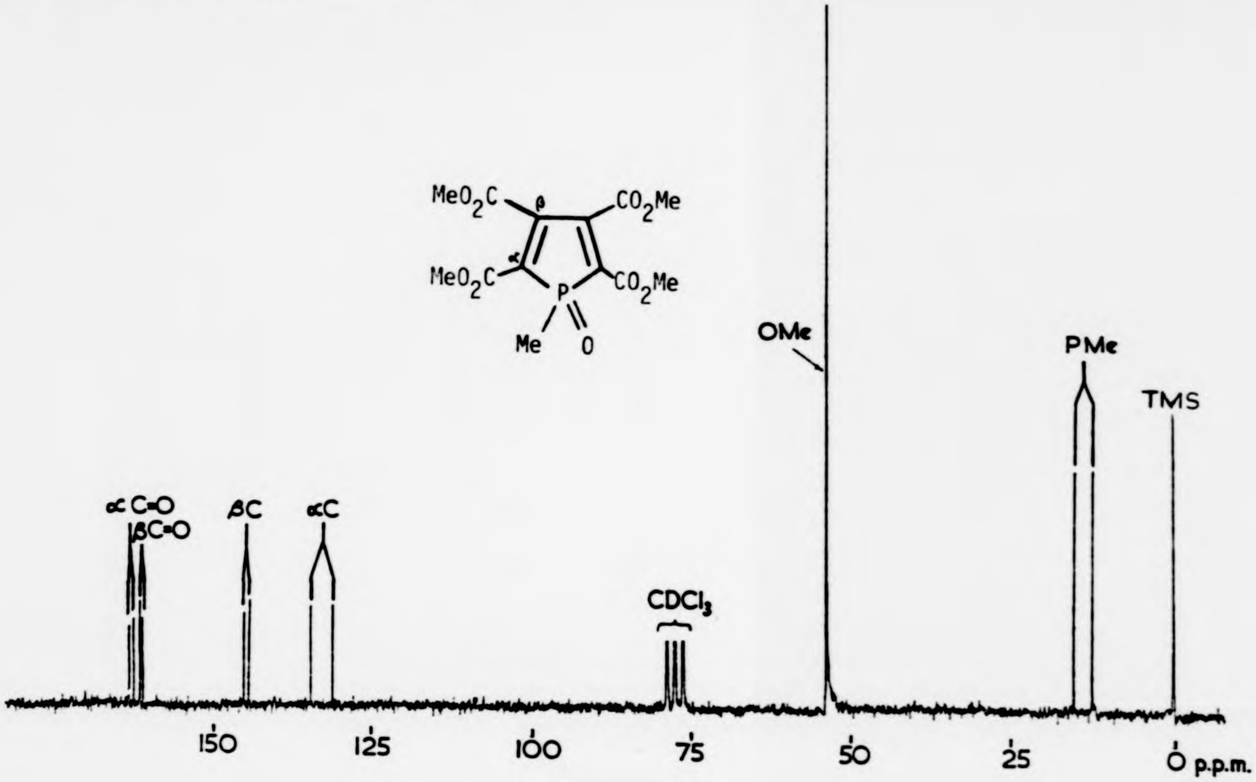
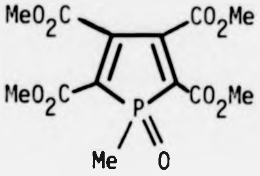


Plate 13

TABLE 22

^{13}C N.m.r. spectral data.

Tetramethyl 1-Methoxy-1-oxo-1H-1λ^{5}-phosphole-2,3,4,5-tetracarboxylate (112; R' = Me).

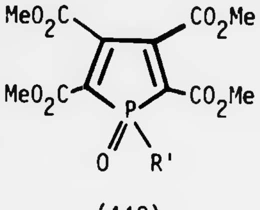


δ(^{13}C)^{a}

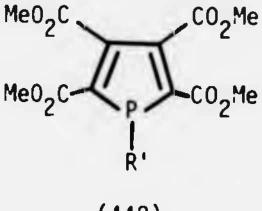
α-C	132.21(87)
β-C	144.20(20)
C=O	160.60(12)
	162.15(18)
OMe	53.36
	53.36
Me	13.69(71)

[a] Shifts in p.p.m. from Me$_4$Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

the presence of triethylamine appeared to be the obvious choice to try initially for the reduction of the oxo-phosphole (112; R' = Ph) since it would be expected to have no effect on the carboxylic esters on the heterocyclic ring.[74b] However, considerable problems were experienced with this particular mixture of reagents.



(112)



(118)

Despite considerable efforts to ensure that the triethylamine was pure there still appeared to be some type of reaction between the amine and the phosphole prior to addition of the trichlorosilane. Furthermore, the product after addition of the trichlorosilane showed numerous ^{31}P n.m.r. signals.

The use of both N-methyl piperidine and pyridine was therefore investigated as an alternative to the triethylamine. However, while these had no effect on the oxo-phosphole (112; R' = Ph) the subsequent addition of the trichlorosilane again led to the formation of a large number of products.

The decomposition of the oxo-phosphole (112; R' = Ph) was even more marked when lithium aluminium hydride was used as the reducing agent.

Although lithium aluminium hydride was expected to reduce the carboxylic esters in the oxo-phosphole (112; R ' = Ph) as well as the phosphoryl group, these reactions could not account for the number of products formed. The product from lithium aluminium hydride gave a considerable number of signals in the ^{31}P n.m.r. spectrum in the range δ_P 43.6 to 16.6 p.p.m. together with two additional signals, one at δ_P 1.7 and the other at δ_P -122.5 p.p.m. In addition this latter high-field component gave a proton-coupled signal which was a large triplet (J_{PH} 201 Hz). This size of coupling is indicative of a one-bond $^1J_{PH}$ coupling and shows that this component is a primary phosphine. It would therefore seem likely that the phosphine produced was phenylphosphine. Phenylphosphine has been reported to have a ^{31}P n.m.r. chemical shift in the range δ_P 123.8-118.7 p.p.m. and to exhibit a $^1J_{PH}$ coupling of 195-201 Hz. Deeming and Shaw,[75] report values of δ_P 123.5 p.p.m. and $^1J_{PH}$ 201 Hz for phenylphosphine, in very good agreement with those for the component formed by the reduction of the oxo-phosphole (112; R' = Ph).

In view of the susceptibility of such phosphines to oxidation it would thus seem likely that the signal at $\delta(^{31}P)$ 1.7 p.p.m. arises from the oxidation of the phenylphosphine, and is thus phenylphosphine oxide.

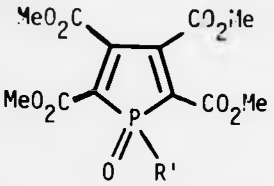
These observations would therefore suggest that the oxo-phosphole ring system was readily cleaving during the reduction with lithium aluminium hydride. This, together with the known susceptibility of the oxo-phosphole (112; R' = Ph) towards nucleophilic attack, suggests that it may be difficult to find a reagent which will achieve the desired reduction of the oxo-phosphole (112; R' = Ph) to the corresponding phosphole (118; R' = Ph).

4. SUMMARY

We have been able to develop a quick and convenient synthesis of a number of novel oxo-phospholes. Furthermore, we have shown that the preparation of the oxo-phospholes (111; R = alkyl) via the cyclic ylides (91; R = alkyl) has a number of advantages over the route originally developed using the low temperature trapping of the n^5-phosphole intermediates (95; R = alkyl).

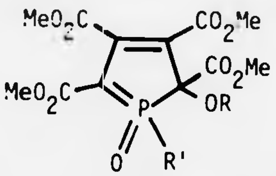
We have also been able to extend the scope of the reaction route via the cyclic ylides (100) to include the preparation of oxo-phospholes such as (112; R' = alkyl or aryl), which, in the case of (112; R' = Me) was previously unavailable in significant quantities by the low temperature trapping route.

We have, however, been unsuccessful in our attempts to form the phospholes such as (118; R' = Ph) by reduction of the corresponding oxo-phospholes (112; R' = Ph). This we believe to be due in large part to the susceptibility of the oxo-phosphole ring to nucleophilic attack.



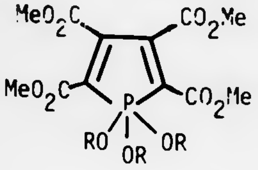
(112)

or (111; R' = OR)

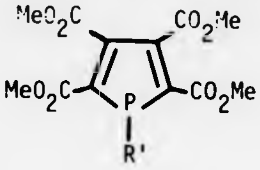


(100)

or (91; R' = OR)



(95) R = alkyl



(118) R' = aryl

CHAPTER 3

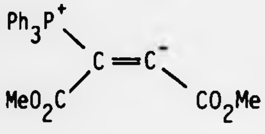
The Incorporation of Carbon Dioxide into Novel Compounds using Organophosphorus Intermediates.

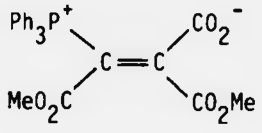
A. *The reaction of trivalent phosphorus compounds with dimethyl acetylenedicarboxylate in the presence of carbon dioxide.*

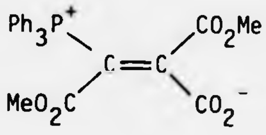
1. INVESTIGATION OF THE PRODUCT FORMED FROM THE REACTION OF TRIPHENYLPHOSPHINE AND DIMETHYL ACETYLENEDICARBOXYLATE IN THE PRESENCE OF CARBON DIOXIDE.

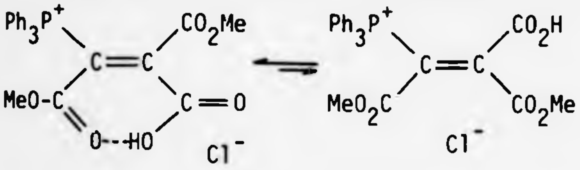
The reaction of carbon dioxide with the 1:1 intermediate (29) initially formed in the reaction between triphenylphosphine and dimethyl acetylenedicarboxylate has been known for many years.[2] Johnson and Tebby had noticed that a pale yellow solid was formed when triphenylphosphine was added to a solution of dimethyl acetylenedicarboxylate in diethyl ether, cooled in an acetone/CO_2 cooling bath. It was clear from the combustion analysis of this material that it contained additional carbon over that provided by the phosphine and acetylenic ester and the source of this carbon was eventually traced to the carbon dioxide from the cooling bath. This observation clearly highlighted the reactivity of the 1:1 intermediate (29) towards carbon dioxide.

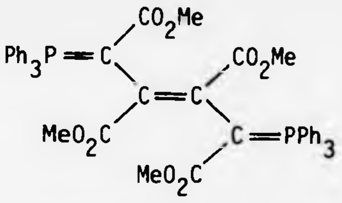
From the evidence obtained it was proposed that the adduct produced from the reaction of the 1:1 intermediate (29) with carbon dioxide, the "CO_2-adduct", had the betaine structure (31) although the possibility that the material was present as both the cis and trans isomers (119 and 31) was not ruled out. Thus, for example, the CO_2-adduct gave a mixture of both dimethyl fumarate and dimethyl maleate in addition to triphenylphosphine oxide on hydrolysis.[4] Furthermore, it was observed that treatment of the CO_2-adduct with anhydrous hydrogen chloride led to the formation of a chloride salt whose infra-red spectrum was interpreted as indicating the presence of both cis and trans isomers (32 and 32b).[21]

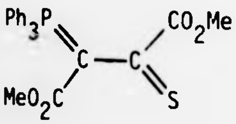

(29)


(119)


(31)


(32b) (32a)


(68)


(34)

It was shown that in solution the CO_2-adduct decomposed with the evolution of carbon dioxide to apparently regenerate the 1:1 intermediate (29). Thus, in the absence of trapping reagents the decomposition of the CO_2-adduct was shown to lead to the formation of the 1,4-diphosphorane (68),[21] presumably by attack of the regenerated 1:1 intermediate on the intact CO_2-adduct (31). On the other hand, it has been shown that in the presence of sulphur the regenerated

1:1 intermediate reacts to give 1,2-bis(methoxycarbonyl)-2-thioxoethylidenetriphenylphosphorane (34),[15] the same product as that obtained when triphenylphosphine was added to dimethyl acetylenedicarboxylate in the presence of sulphur.

We have investigated the preparation of the CO_2-adduct from triphenylphosphine and dimethyl acetylenedicarboxylate as part of our studies into the reactions of trivalent phosphorus compounds with electrophilic acetylenes, and have determined its ^{31}P n.m.r. chemical shift. Rather surprisingly, the ^{31}P n.m.r. chemical shift of the adduct was found to be 0.29 p.p.m. which is at considerably higher field than that expected for the carboxylate betaine structure (31) originally proposed. Phosphonium salts are usually observed to have ^{31}P n.m.r. chemical shifts in the region of δ_P 20 to 45 p.p.m.[58] Furthermore, the presence of only one resonance line in the ^{31}P n.m.r. spectrum of the CO_2-adduct clearly showed that only one isomeric form was present in solution.

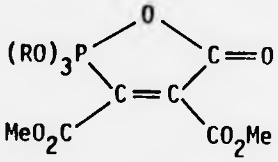
To explain the upfield shift of the ^{31}P n.m.r. signal from the CO_2-adduct it is necessary to propose that there is some degree of association between the phosphonium and carboxylate centres in the adduct. However, if we were to propose a formal covalent bond between these two centres to give a pentacovalent phosphorane, such as (120), this would be equally unacceptable. Compounds of this type characteristically have high field shifts in the ^{31}P n.m.r. spectrum in the region δ_P -85 to -100 p.p.m.[59]

It is necessary therefore to postulate that there is some degree of covalent character in the association between the phosphonium and carboxylate centres as in structure (121).

TABLE 23

^{31}P N.m.r. spectral data.

2,2,2-Trimethoxy-3,4-bis(methoxycarbonyl)-5-oxo-Δ^3-oxaphospholene (108).



(108)

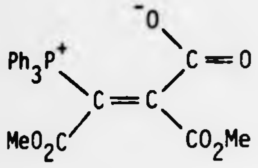
R	δ[a]
Me	-50.90[b]
Et	-53.69[c]
Pr^i	-56.56[d]

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; [^{2}H]Chloroform, 26 °C.

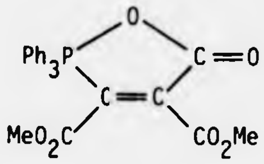
[b] For 3,4-bis(ethoxycarbonyl)-2,2,2-trimethoxy-5-oxo-Δ^3-oxaphospholene. $\delta(^{31}P)$ -52.97 p.p.m.; proton-coupled spectrum, sept, $^3J_{PH}$ 8 Hz; [^{2}H]Chloroform, 26 °C.

[c] Literature value: $\delta(^{31}P)$ -53.8 p.p.m.[22]

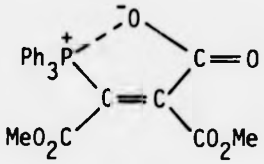
[d] [$^2H_8$]Toluene, 26 °C; proton-coupled spectrum, quartet, $^3J_{PH}$ 9 Hz.



(119)



(120)

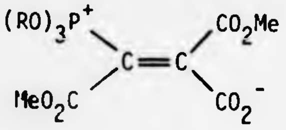


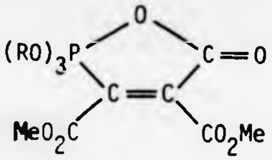
(121)

This in turn implies that the molecule must adopt a <u>cis</u> arrangement at the double bond.

2. THE REACTION OF CARBON DIOXIDE WITH THE 1:1 INTERMEDIATE FORMED IN THE REACTION OF DIMETHYL ACETYLENEDICARBOXYLATE WITH OTHER TRIVALENT PHOSPHORUS COMPOUNDS.

We were interested to see whether it was possible to increase the covalent character of the link between the phosphonium and carboxylate centres in the "CO_2-adducts" such as (121), formed by the reaction of carbon dioxide with the 1:1 intermediate (29), by increasing the electronegativity of the substituents on the phosphorus atom. We have investigated this by progressively replacing the phenyl groups on the phosphorus by methoxy groups. As expected, the replacement of even only a single phenyl group by a methoxy group did markedly increase the degree of covalent character in the interaction between the phosphonium and carboxylate centres. This was clearly indicated by the ^{31}P n.m.r. chemical shifts of the CO_2-adducts. Thus, the CO_2-adducts from methyl diphenylphosphinite, dimethyl phenylphosphonite, and trimethyl phosphite all showed high field chemical shifts at $\delta(^{31}P)$ -40.9, -37.0, and -50.9 p.p.m. respectively (see Table 23 and 24). The ^{31}P n.m.r. chemical shifts of other CO_2-adducts are also given in Tables 23 and 24, thus illustrating the range of the CO_2-adducts formed. However, while the adducts from methyl diphenylphosphinite and dimethyl phenylphosphonite were produced cleanly, that from trimethyl phosphite was always associated with signals at $\delta(^{31}P)$ 47.4 and 2.33 p.p.m. Although it was initially felt that the low field signal might correspond to the previously unobserved trans system (123) it was quickly established that this material was being produced by the reaction of the initially formed CO_2-adduct (108; R = Me) with trimethyl phosphite.[64]


(123)


(108)

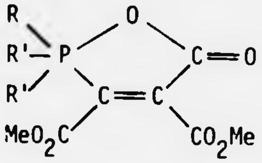
The addition of two molar equivalents of trimethyl phosphite to one of the dimethyl acetylenedicarboxylate in chloroform in the presence of a plentiful supply of carbon dioxide led to the formation of a reaction mixture containing only the signals at $\delta(^{31}P)$ 47.4 and 2.33 p.p.m. It was quickly established that both these signals were decets in the proton-coupled ^{31}P n.m.r. spectrum and hence the signal at δ_P 2.33 p.p.m. was readily identified as being trimethyl phosphate. However, the remaining signal, that at δ_P 47.4 p.p.m. was more difficult to identify. Griffiths and Tebby had carried out a preliminary investigation into the nature of this component shortly before the commencement of this study.[22] They had shown that this compound at δ_P 40.4 p.p.m. in the ^{31}P n.m.r. spectrum still had three alkoxy groups attached to the phosphorus atom and since its ^{13}C n.m.r. spectrum showed a characteristically large phosphorus coupling to the α-carbon [$^{1}J_{PC}$ = 250 Hz] that it must be an ylide. They were also able to show that the addition of trimethyl phosphite to the CO_2-adduct from triethyl phosphite led to the formation of some triethyl phosphate[64] indicating that the phosphate formed in the reaction was derived originally from the phosphorus in the CO_2-adduct. The phosphorus in the CO_2-adduct was thus being displaced during the reaction. We have been able to show this even more conclusively since we have shown that it is possible to generate the ylide at $\delta(^{31}P)$ 47.44 p.p.m. by treating the CO_2-adduct from dimethyl phenylphosphonite (122; R = Ph, R' = OMe) (see Table 24) with trimethyl phosphite. The formation of dimethyl phenylphosphonate clearly indicated the loss of the phosphorus atom from the initial CO_2-adduct (112; R = Ph, R' = OMe). Since the oxygen from the carboxylate centre is effectively covalently bonded to the phosphorus atom in the CO_2-adduct from dimethyl phenylphosphonite it would seem reasonable to assume that the source of the oxygen in the dimethyl phenylphosphonate is this carboxylate oxygen.

The ^{13}C n.m.r. spectrum of the ylide giving a signal at $\delta(^{31}P)$ 47.4 p.p.m. is given in Table 25. This ^{13}C n.m.r. data was originally interpretated[64] as showing the presence of two ester groups. This interpretation was supported by the observation that the reaction of the ylide with 4-nitrobenzaldehyde led to the formation of a furan bearing two adjacent ester groups (this reaction is discussed in more detail later). The presence of the two adjacent ester groups on the furan in turn led to the conclusion that the dimethyl acetylenedicarboxylate had been incorporated into the furan without cleavage or rearrangement

TABLE 24

^{31}P N.m.r. spectral data.

3,4-Bis(methoxycarbonyl)-5-oxo-Δ^3-oxaphospholene.



(121) R,R' = Ph.

(122) R = Ph, R' = OEt, OMe.

R = OMe, R' = Ph

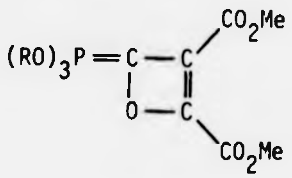
R	R'	δ^a
Ph	OEt	-38.53
Ph	OMe	-37.05
OMe	Ph	-40.92
Ph	Ph	0.29[b]

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; [^{2}H]Chloroform, 26 °C.

[b] A formal covalent bond between the phosphorus and the oxygen of the 1,2-oxaphospholene ring does not exist [see earlier discussion].

TABLE 25

^{13}C N.m.r. spectral data.

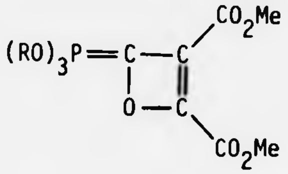


(124; R = Me)

δ^a	R = Me
R	55.49(6)
Me	50.46
	56.95
α-C	47.67(251)
β-C	86.09(15)
γ-C	154.52(21)
β-C=0	163.29(26)
γ-C=0	163.45

[a] Shifts in p.p.m. from Me$_4$Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

and hence it was reasonable to conclude that it had been incorporated into the ylide precursor in a similar manner. The structure (124) (see Table 25) was therefore proposed for the ylide generated from the reaction of two molar equivalents of trimethyl phosphite with dimethyl acetylenedicarboxylate in the presence of carbon dioxide.

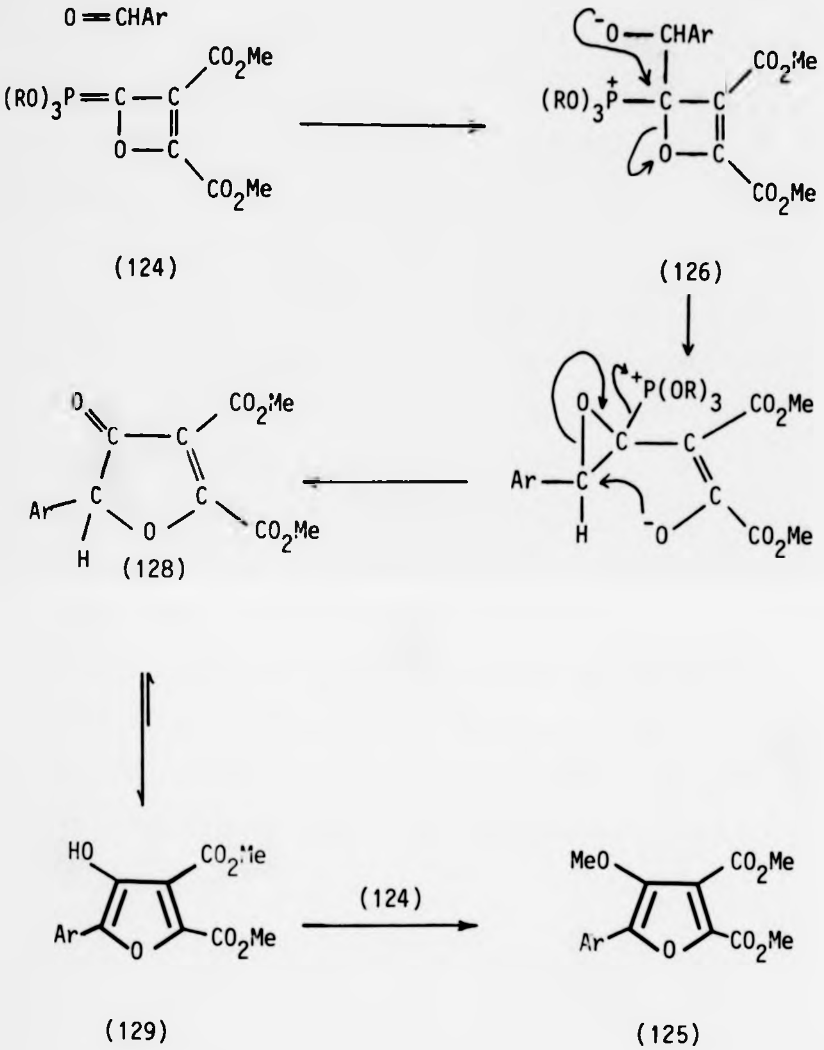


(124)

3. THE FORMATION OF NOVEL FURANS FROM THE REACTION OF ALDEHYDES WITH THE YLIDE GENERATED FROM THE "CO_2-ADDUCT" (108).

3.1 <u>The reaction of 4-nitrobenzaldehyde with the ylide generated from the reaction of trimethyl phosphite with dimethyl acetylenedicarboxylate in the presence of carbon dioxide</u>.

Using the proposed structure for the ylide (124) generated using carbon dioxide Griffiths and Tebby[22] were able to rationalise the formation of the furan (125) in the reaction of the ylide (124; R = Me) with 4-nitrobenzaldehyde, as shown in Fig. 28.

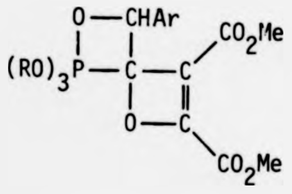


Ar = 4-$NO_2C_6H_4^-$

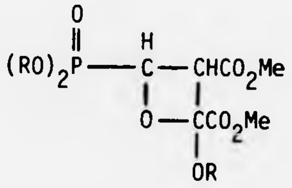
R = Me

Fig. 28 [22]

The mechanism proposed the initial formation of the betaine (126). The reaction, however, did not subsequently follow the normal Wittig type pathway. It was suggested that this might be due to the unfavourable situation which would be present in the resulting oxaphosphetane (127), where a highly strained spiro-system would be formed. Instead, if was proposed that a cyclisation took place to give the furanone ring (128) via nucleophilic attack on the transient epoxide formed. Keto-enol tautomerism would then be expected to give rise to the more favourable unsaturated furan system (129) and alkylation would then occur by dealkylation of a molecule of the ylide (124; R = Me). Support for this mechanism was obtained by the observation of the simultaneous formation of trimethyl phosphite and a component giving a ^{31}P n.m.r. signal at about δ_P 21.3 p.p.m. which was consistent with the formation of the phosphonate (130; R = Me). Furthermore, by varying the nature of the ester groups on both the acetylenic ester and the phosphite it was clearly shown that the alkoxy substituent on the furan was derived from the trialkyl phosphite.

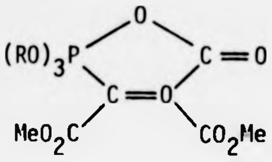


(127)

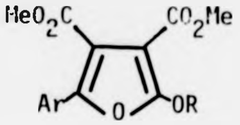


(130)

Although Griffiths and Tebby were aware that the isomeric furan (131; R = Me) could also account for the observed spectroscopic data they felt that this structure was probably less likely from a mechanistic point of view.[64] It was clear that this was a point which needed to be clarified as soon as possible and therefore we decided to synthesise one of the two possible furan structures, so that it could be compared with the furan formed via the CO_2-adduct (108; R = Me). Since the isomeric furan (131; R = Me) seemed more amenable to synthesis it was this system which was initially chosen for preparation by an independent synthetic route.



(108)



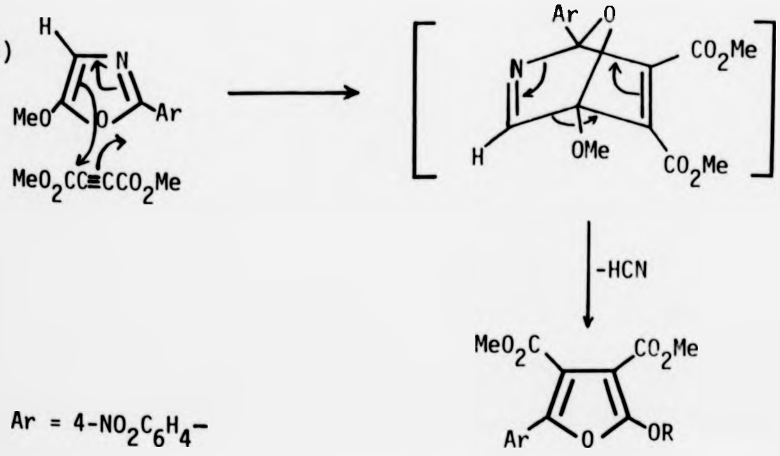
Ar = 4-$NO_2C_6H_4$-

(131)

3.2 The independent synthesis of dimethyl 5-methoxy-2-(4-nitrophenyl)-furan-3,4-dicarboxylate (131; R = Me).

The route chosen for the synthesis of the furan was that shown in Fig. 29. This route has been used successfully for the synthesis of a number of similar furans.[65]

(133)

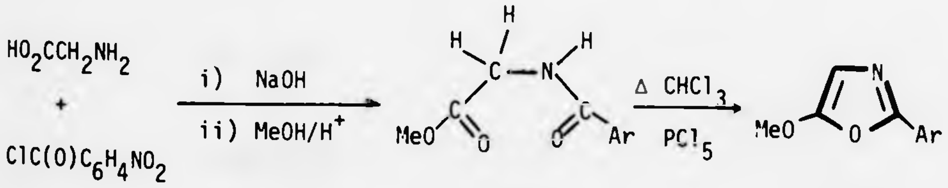


Ar = 4-$NO_2C_6H_4$-

(131; R = Me)

Fig. 29

The method involves the Diels-Alder addition of a suitably substituted oxazole to the acetylenic dicarboxylic ester to form an oxabicyclo-azahexadiene system (132) which spontaneously eliminates hydrogen cyanide to give the furan (131; R = Me), dimethyl 5-methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate. The preparation of the furan (131; R = Me) initially involved benzoylation of glycine to give the N-substituted glycine (134) which was then esterified in essentially quantitative yield by treatment with methanolic sulphuric acid. Difficulties were encountered in effecting the cyclisation of the N-substituted glycine (134) by dehydration to give the oxazole (133). A variety of reagent and conditions were attempted including Dean-Stark dehydration, and heating an intimate mixture of the glycinate with phosphorus pentoxide and phosphorus pentachloride both in the presence and absence of solvents. Depending on the reaction conditions these reactions either led to the reisolation of the unreacted glycinate (134) or to the formation of polymeric material.



(134)

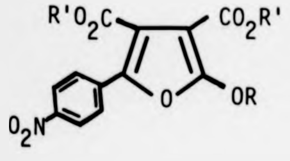
(133)

Ar = $pC_6H_4NO_2$

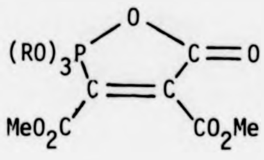
Eventually it was found that heating the glycinate (134) with phosphorus pentachloride under reflux in chloroform over 2 days effected cyclisation to give the oxazole (133) in good yield. Monitoring the course of the reaction by ^1H n.m.r. spectroscopy enabled us to see that extending the period of heating under reflux led to decomposition of the oxazole (133). The oxazole (133), 5-methoxy-2-(4-nitrophenyl)oxazole, was then heated under a variety of conditions with both dimethyl and diethyl acetylenedicarboxylate in an endeavour to effect the desired Diels-Alder reaction. The conditions reported in the literature[65,66] for this type of reaction were found to be ineffective for the oxazole (133). The oxazole was eventually heated at 120 °C with a ten-fold excess of dimethyl acetylenedicarboxylate in the absence of any other solvent. The progress of the reaction was monitored by ^{1}H n.m.r. spectroscopy and over a period of 12 h. the signal from the olefinic proton in the oxazole (133) at 6.27 p.p.m. gradually disappeared. Changes in the AA'BB' system corresponding to the para-substituted phenyl ring in the oxazole (133) were also seen as the reaction proceeded. At the end of the reaction the dimethyl acetylenedicarboxylate was distilled off and the residue recrystallised from toluene to give the desired furan (131; R = Me), albeit in low yield (about 13%). The ^{13}C n.m.r. spectrum is given in Table 26 (Plate 14).

3.3 The structure and range of furans prepared via the route involving carbon dioxide.

The furan (131; R = Me) prepared from the reaction of 5-methoxy-2-(4-nitrophenyl)oxazole (133) with dimethyl acetylenedicarboxylate was found to be spectroscopically identicial to that prepared via the route involving the CO_2-adduct (108; R = Me) from trimethyl phosphite and dimethyl acetylenedicarboxylate (see Table 26 and Plate 14). The melting points were also the same as was the mixed melting point.



(131)

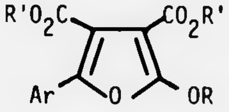


(108)

TABLE 26

^{13}C N.m.r. spectral data

Dimethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate.



(131)

Ar = 4-$C_6H_4NO_2$

δ^a	R, R' = Me	
R	58.74	(q, 140)
R'	51.88	(q, 147)
	53.14	(q, 147)
C-2	146.66	(t)[b]
C-3	118.65	(s)
C-4	93.31	(s)
C-5	161.25	(q, 4)
C=O	161.51	(q, 4)
	164.23	(q, 4)
Ar	124.07	(d of d; 5, 170)
	125.04	(d of d; 7, 167)
	134.03	(t, 8)
	138.78	(t, 4)

[a] Shifts in p.p.m. from Me_4Si; multiplicity and J_{CH} from proton-coupled spectrum in Hz in parentheses; [^2H]Chloroform, 26 °C.

[b] Additional coupling present, signal broadened.

^{13}C N.m.r. spectrum of dimethyl 5-methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Me) (proton decoupled).

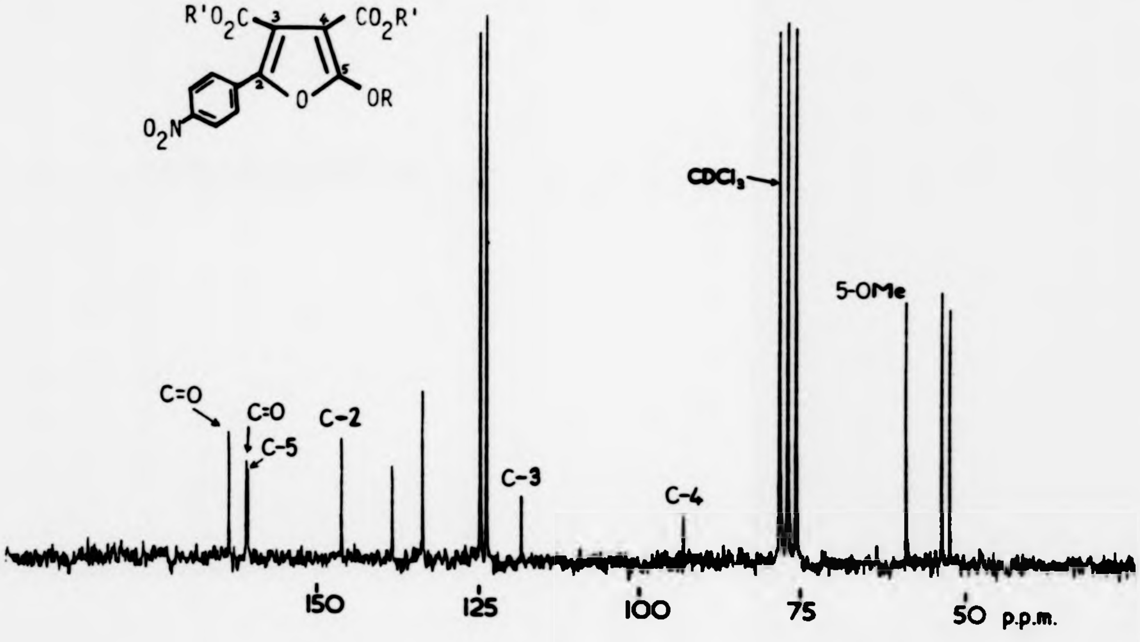


Plate 14

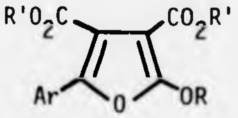
It is interesting to compare at this point the relative ease of preparation of the furan (131; R = Me) by the two routes. In the case of the reaction involving the CO_2-adduct (108; R = Me) the overall yield of the furan (131; R = Me) (67%) (see Table 27) was considerably higher and the procedure considerably quicker and easier than the route involving the formation of the oxazole (see Fig. 29). Although the preparation of the oxazole (133) proceeded in good yield the subsequent Diels-Alder reaction and elimination steps (see Fig. 29) occurred in poor yield (13%; overall yield 6%). The range of furans prepared via the CO_2-adducts (108; R = alkyl) from the reaction of trialkyl phosphites and dimethyl or diethyl acetylenedicarboxylate with carbon dioxide is given in Table 27. The ^{13}C n.m.r. spectrum of the analogues of the furan (131; R = Me) prepared are given in Tables 28 and 29 [for ^{1}H n.m.r. spectral details see Experimental section].

4. THE STRUCTURE OF THE YLIDE FORMED FROM THE REACTION OF THE "CO_2-ADDUCT" (108; R = Me) WITH TRIMETHYL PHOSPHITE.

At the same time as we were developing the route for the synthesis of the furan (131; R = Me) we were also engaged in a study of the reactions of the ylide formed from the CO_2-adduct (108; R = alkyl) which had been assigned the structure (124; R = alkyl) for the reasons previously discussed. During these investigations it became clear that some of the reactions of the ylide were difficult to rationalise on the basis of the originally proposed structure (124). Thus, for example, the reaction of the ylide (124) with an alcohol such as methanol led to the formation of two components which gave ^{31}P n.m.r. shifts at 60.4 and 58.5 p.p.m. The proton-coupled ^{31}P n.m.r. spectrum of these components (decet)

TABLE 27

Dialkyl 5-Alkoxy-2-(aryl)furan-3,4-dicarboxylates (131)[a].



(131)

R	R'	YIELD (%)
Me	Me	67.3
Me	Me	13.0[b]
Me	Et	78.8
Me	Et	9.1[b]
Et	Me	54.1
Et	Et	46.4
Pr^i	Me	40.1
Me	Me	54.6[c]
Me	Me	17.0[d]

[a] Ar = 4-nitrophenyl unless otherwise stated.

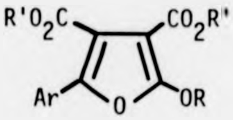
[b] Prepared from 5-methoxy-2-(4-nitrophenyl)oxazole.

[c] Ar = 4-bromophenyl [see Experimental section].

[d] Prepared from the reaction of the CO_2-adduct (122; R = Ph, R' = Me), from dimethyl phenylphosphonite and dimethyl acetylenedicarboxylate, with 4-nitrobenzaldehyde [see Experimental section].

TABLE 27

Dialkyl 5-Alkoxy-2-(aryl)furan-3,4-dicarboxylates (131)[a].



(131)

R	R'	YIELD (%)
Me	Me	67.3
Me	Me	13.0[b]
Me	Et	78.8
Me	Et	9.1[b]
Et	Me	54.1
Et	Et	46.4
Pr^i	Me	40.1
Me	Me	54.6[c]
Me	Me	17.0[d]

[a] Ar = 4-nitrophenyl unless otherwise stated.

[b] Prepared from 5-methoxy-2-(4-nitrophenyl)oxazole.

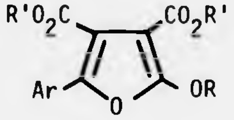
[c] Ar = 4-bromophenyl [see Experimental section].

[d] Prepared from the reaction of the CO_2-adduct (122; R = Ph, R' = Me), from dimethyl phenylphosphonite and dimethyl acetylenedicarboxylate, with 4-nitrobenzaldehyde [see Experimental section].

TABLE 28

^{13}C N.m.r. spectral data.

Diethyl 5-Ethoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R = Et, R' = Me).



(131)

δ^a	R = Et, R' = Me	
R	14.93	(q, 127)
	68.81	(t of q; 147, 4)
R'	51.70	(q, 147)
	52.96	(q, 147)
C-2	146.51	(t)[b]
C-3	118.37	(s)
C-4	93.81	(s)
C-5	160.88	(br.t)
C=O	161.46	b
	164.21	(q, 5)
Ar	123.92	(d of d; 4, 170)
	124.94	(d of d; 7, 167)
	134.0	(t, 8)
	138.58	(t, 4)

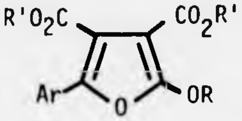
[a] Shifts in p.p.m. from Me_4Si; multiplicity and J_{CH} from proton-coupled spectrum in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] Additional coupling present, signal broadened.

TABLE 28 continued

^{13}C N.m.r. spectral data

Diethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R = Me, R' = Et).



(131)

δ^a	R = Me, R' = Et	
R	58.60	(q, 137)
R'	13.96	(q, 128)
	14.22	(q, 128)
	60.52	(t of q; 138, 4)
	62.13	(t of q; 138, 4)
C-2	146.41	(t)[b]
C-3	118.83	(s)
C-4	93.52	(s)
C-5	161.24	(q, 4)
C=O	160.91	(t, 3)
	163.65	(t, 3)
Ar	123.89	(d of d; 6, 170)
	124.82	(d of d; 6, 170)
	130.06	(t, 8)
	138.26	(t, 6)

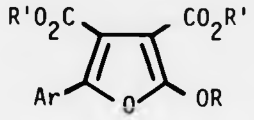
[a] Shifts in p.p.m. from Me_4Si; multiplicity and J_{CH} from proton-coupled spectrum in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] Additional coupling present, signal broadened.

TABLE 28 continued

^{13}C N.m.r. spectral data.

Dimethyl 2-(4-nitrophenyl)-5-isopropoxyfuran-3,4-dicarboxylate (131; R = Pr^{i}, R' = Me).



(131)

δ^{a}	R = Pr^{i}, R' = Me	
R	22,37	(q, 128)
	78.33	(d of sept; 149, 4)^{b}
R'	51.70	(q, 148)
	52.99	(q, 148)
C-2	146.55	(t)^{b}
C-3	118.19	(s)
C-4	95.11	(s)
C-5	160.66	(d, 2)
C=O	161.60	(q, 4)
	164.38	(q, 4)
Ar	123.98	(d of d; 5, 170)
	125.05	(d of d; 7, 167)
	134.12	(t, 8)
	138.84	(br. t; 4)

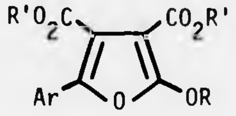
[a] Shifts in p.p.m. from Me$_4$Si; multiplicity and J_{CH} from proton-coupled spectrum in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] Additional coupling present, signal broadened.

TABLE 28 continued

^{13}C N.m.r. spectral data.

Diethyl 5-Ethoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Et).



(131)

δ^a	R, R' = Et	
CH_3	13.98	(q, 127)
	14.22	(q, 127)
	14.93	(q, 127)
CH_2	60.47	(t, q; 147, 4)
	62.13	(t, q; 148, 4)
	68.84	(t, q; 149, 4)
C-2	146.43	(t, 3)[b]
C-3	118.69	(s)
C-4	94.20	(s)
C-5	161.02	(t, 4)[c]
C=O	161.02	(t, 4)[c]
	163.80	(t, 3)
Ar	123.92	(d,d; 170, 5)
	124.86	(d,d; 167, 7)
	134.18	(t, 8)
	138.31	(t, 4)

[a] Shifts in p.p.m. from Me_4Si; multiplicity and J_{CH} from proton-coupled spectrum in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

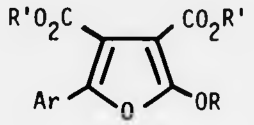
[b] Additional coupling present, signal broadened,

[c] Superimposed signals.

TABLE 29

^{13}C N.m.r. spectral data.

Dimethyl 2-(4-bromophenyl)-5-methoxyfuran-3,4-dicarboxylate (131; R,R' = Me).



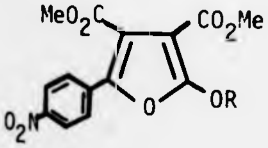
(131) Ar = 4-BrC_6H_4

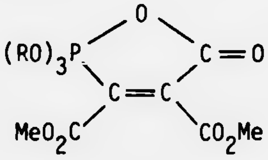
δ[a]	R,R' = Me	
OMe	51.60	(q, 147)
	52.67	(q, 148)
	58.46	(q, 148)
C-2	140.65	(br)
C-3	115.28	(s)
C-4	92.50	(s)
C-5	160.44	(q, 4)
C=0	161.70	(q, 4)
	164.38	(q, 4)
Ar	122.36	(t)
	126.49	(d,d; 3, 163)
	127.10	(t)
	131.60	(d,d; 3, 163)

[a] Shifts in p.p.m. from Me_4Si; multiplicity and J_{CH} from proton-coupled spectrum in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

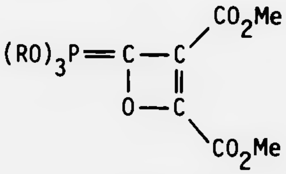
[see later Discussion] clearly showed that three methoxy groups still remained attached to the phosphorus atoms while the ^{13}C n.m.r. spectrum [see later Discussion] showed the presence of non-protonated carbon atoms adjacent to the phosphorus atoms in both components. These carbon atoms also exhibited large $^{1}J_{PC}$ couplings of about 230 Hz which we have come to accept as being indicative of an ylidic carbon.

The treatment of the original ylide, previously proposed to be (124; R = Me) with methanol had thus led to the protonation of the carbon adjacent to the ylidic carbon, thus resulting in the formation of a new ylide which was stable in the presence of methanol. This latter behaviour was consistent with the formation of a highly stabilised ylide on treatment of the original ylide with methanol and clearly indicated that the originally proposed structure (124) was unacceptable. It was felt that this would also explain why the furan (131; R = Me) produced on treatment of the ylide (124; R = Me) with 4-nitrobenzaldehyde had been one which was difficult to rationalise from a mechanistic point of view.





(108)



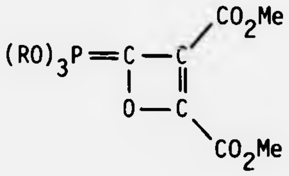
(124)

In order to obtain further information about the ylide originally proposed to be (124), it was therefore decided to carry out a study to determine the fate of the carbon dioxide which was incorporated into the ylide. To do this it was necessary to use ^{13}C enriched carbon dioxide.

5. STUDIES USING ^{13}C ENRICHED CARBON DIOXIDE.

5.1 Introduction.

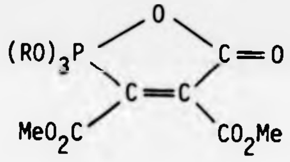
The use of isotopically labelled compounds to elucidate reaction mechanisms is well established. Since the natural abundance of the ^{13}C nucleus is only 1.108% the incorporation of a ^{13}C atom into a molecular can readily be identified by ^{13}C n.m.r. spectroscopy, the isotopically enriched site giving an enhanced signal intensity relative to that in the corresponding non-isotopically enriched system. Furthermore, if the level of ^{13}C isotopic enrichment is sufficiently high at a given carbon, then coupling between this ^{13}C atom and the adjacent ^{13}C atoms will become apparent [see Introduction]. This will result in the splitting of those natural abundance ^{13}C resonance lines from carbon atoms adjacent to the site of ^{13}C labelling. By incorporating isotopically labelled carbon dioxide into the ylide [originally assigned the structure (124)] it was thus hoped to be possible to not only identify the site of labelling, but to also identify the adjacent carbon atoms.



(124)

5.2 Investigation of the use of "static" conditions in the generation of the CO_2-adduct.

The major problem associated with the use of ^{13}C labelled carbon dioxide for the study of the CO_2-adduct (108) stemmed from the fact that the labelled gas was supplied at atmospheric pressure in a glass ampoule. All previous work by us with carbon dioxide had involved bubbling the gas through one reactant while slowly adding the other reactant. This was clearly not possible with a limited volume of expensive isotopically labelled carbon dioxide. It was therefore necessary to develop a procedure which would enable the carbon dioxide to be used under essentially "static" conditions, but which at the same time would ensure that carbon dioxide would be present when the trialkyl phosphite reacted with the dimethyl acetylenedicarboxylate, so avoiding undesirable side reactions.

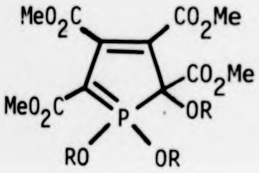


(108)

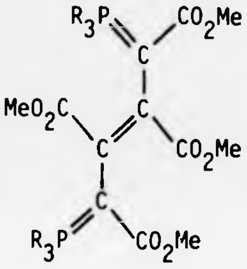
5.3 Trapping reactions using a limited volume of carbon dioxide.

The investigation into whether the "CO_2 trapping reaction" was possible under "static" conditions was first carried out using non-enriched carbon dioxide. Early work was disappointing since reaction products containing numerous phosphorus-containing components were obtained. On one occasion when two molar equivalents of trimethyl phosphite were added to one of dimethyl acetylenedicarboxylate in the presence of carbon dioxide, the ^{31}P n.m.r. spectrum of the reaction product showed the presence not only of trimethyl phosphate, 1,1,2-trimethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Me), and unreacted trimethyl phosphite, but also a component having a ^{31}P n.m.r. chemical shift of δ_P 52.58 p.p.m. in [$^2H_8$]toluene. Fortunately, this unidentified component precipitated slowly from the crude reaction mixture over a period of several days. This solid was purified by recrystallisation from toluene and identified by its n.m.r. spectra [see Experimental section] as the 1,4-diphosphorane (68; R = OMe). This is analogous to the product (68; R = Ph) which has been reported to be formed by the decomposition of the CO_2 adduct (31) in solution.[21]

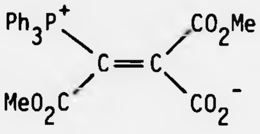
The infra-red spectrum of the 1,4-diphosphorane (68; R = OMe)



(91; R = Me)



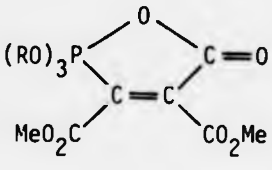
(68)



(31)

showed the presence of two ester carbonyl bonds at 1745 and 1645 cm^{-1}. The low value of the latter carbonyl bond has been observed in other systems where stabilisation of the phosphorane by delocalisation of the charge onto the ester occurs.[4]

However, despite the early difficulties the results of the trapping reactions with "static" carbon dioxide improved. The progress was facilitated by constructing an appropriate reaction vessel [see later description] and by changing the reaction solvent from toluene to deuteriochloroform. The effect of changing the solvent should perhaps have been anticipated. Toluene being a non-polar solvent might have been expected to suppress the formation of the CO_2-adducts (108) which occur via an anionic mechanism while, favouring those which possibly occur via mechanisms where the 1:1 intermediate (87) exhibits more of its carbene character.



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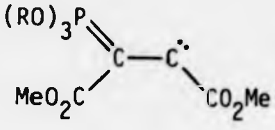


(87)

5.4 Procedure for using limited volumes of carbon dioxide in trapping reactions.

The apparatus used for carrying out the carbon dioxide "trapping reactions" is shown diagrammatically in Fig. 30. It consists of a litre glass ampoule with an extension fitted with a cone for attachment and a 'Rotoflo' gas tap. The reaction vessel (volume 40 cm^3) was fitted with a rubber septum at one end, for the introduction of materials, and a socket and tap at the other for the attachment to the ^{13}C-enriched carbon dioxide reservoir. In the initial reactions using non-enriched carbon dioxide a flask of similar dimensions to that of the ampoule of ^{13}C isotopically--enriched carbon dioxide was used. In order to facilitate the diffusion of the carbon dioxide into the reaction vessel the early experiments were carried out with the reaction flask initially filled with hydrogen. Placing the carbon dioxide reservoir above the reaction vessel prior to opening the connecting tap encouraged the upward motion of the hydrogen and the downward migration of the carbon dioxide into the reaction vessel. However, while this enabled the reaction vessel to be filled efficiently with carbon dioxide of high isotopic enrichment, this procedure clearly led to a gradual dilution of the carbon dioxide in the reservoir by hydrogen. This reduction in the carbon dioxide concentration eventually began to have an adverse

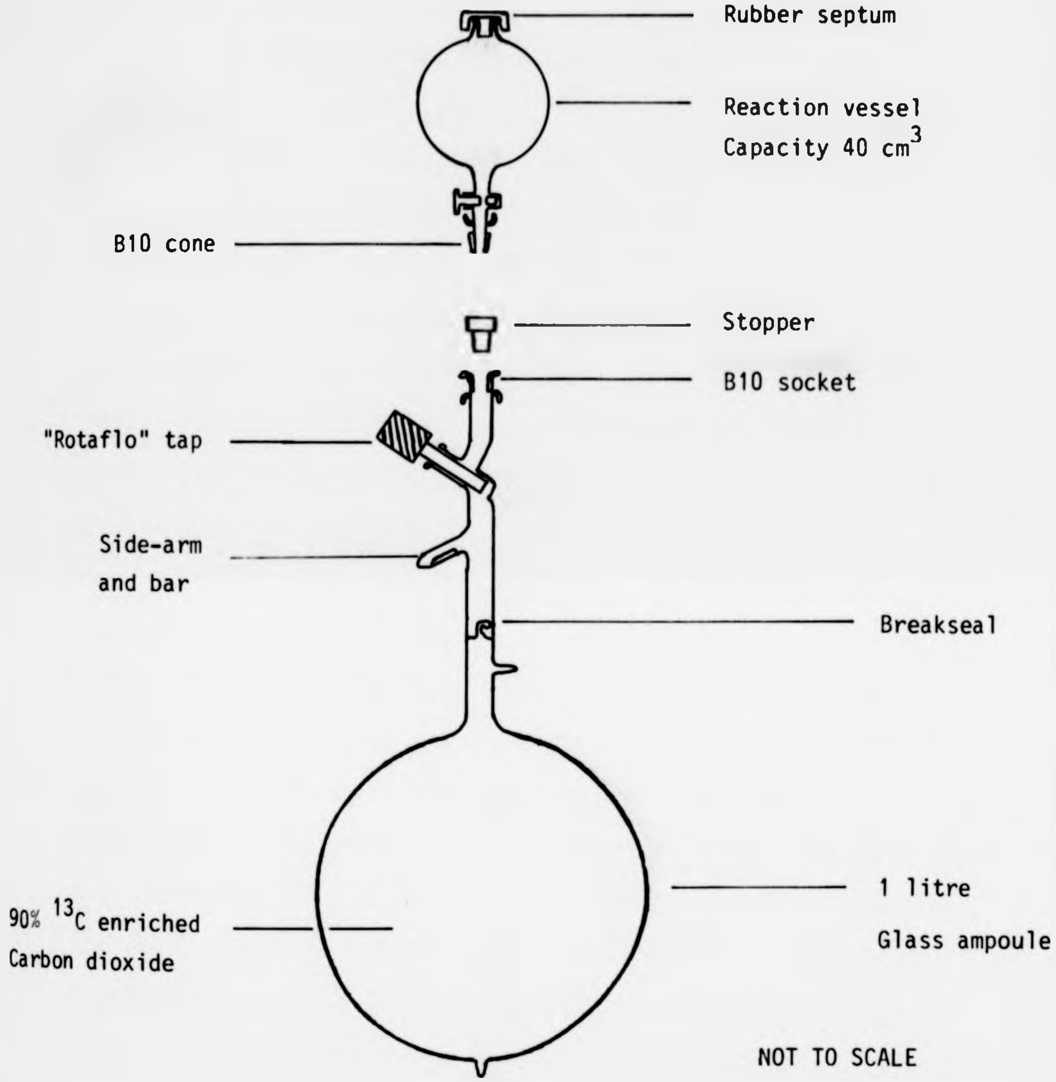

Rubber septum
Reaction vessel
Capacity 40 cm^3
B10 cone
Stopper
B10 socket
"Rotaflo" tap
Side-arm
and bar
Breakseal
1 litre
Glass ampoule
90% ^{13}C enriched
Carbon dioxide
NOT TO SCALE

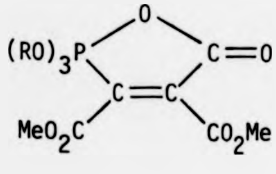
Fig. 30

effect on the trapping efficiency during the reaction. It was therefore decided that since it was not necessary to use 90% ^{13}C isotopic purity carbon dioxide in all our studies that it might be more satisfactory in some circumstances to use non-enriched carbon dioxide in place of the hydrogen. However, this provided some difficulties since on opening the tap between the isotopically enriched carbon dioxide reservoir and the reaction vessel filled with normal carbon dioxide there was no significant incentive for the two gases to diffuse into each other. To encourage this mixing process it was therefore necessary to gently warm one flask while cooling the other in ice and then to reverse this process. This cycle was repeated several times until sufficient mixing was considered to have occurred.

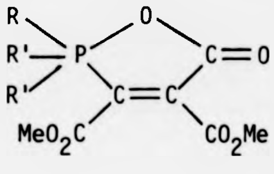
Once the reaction vessel (see Fig. 30) had been charged with ^{13}C isotopically-enriched carbon dioxide it was possible to introduce the reactants. The acetylenic ester in deuteriochloroform was first introduced via the septum using a syringe and needle. The flask was then gently shaken to ensure that this solution became saturated with carbon dioxide. The trivalent phosphorus compound was then added slowly to the reaction mixture also using a syringe and needle. Since there was a reduced pressure generated in the reaction vessel when the trivalent phosphorus compound was added some problems were initially encountered. The partial vacuum in the reaction vessel tended to suck the trivalent phosphorus component into the reaction flask too quickly, with the consequence that there was considerable by-product formation. This problem was overcome by using a long fine needle on the syringe. This afforded considerable resistance to the flow of the liquid into the reaction vessel. As the trivalent phosphorus compound was sucked slowly into the reaction flask it was then a simple matter to shake the contents of the flask to ensure rapid mixing of the reagents, including the carbon dioxide. In this manner it was possible to carry out the carbon dioxide trapping reactions cleanly without the formation of unwanted side reactions.

6. AN INVESTIGATION INTO THE SITE OF INCORPORATION OF ^{13}C ENRICHED CARBON DIOXIDE IN THE "CO_2-ADDUCTS" (108 AND 122).

When the preparation of the CO_2-adduct (108; R = Me) was carried out using ^{13}C enriched carbon dioxide the signal at δ_P -50.9 p.p.m. in the proton-decoupled ^{31}P n.m.r. spectrum was no longer observed as a singlet but as a doublet. The splitting of the doublet (J_{PC} 10 Hz) arose due to coupling between the phosphorus and the site of ^{13}C labelling. The relatively small coupling of J_{PC} clearly indicated that the site of incorporation of the carbon dioxide was some distance from the phosphorus atom as anticipated. In some later experiments where the extent of isotopic enrichment was less marked the signal at δ_P -50.9 p.p.m. was often observed to have "triplet" character. The centre line of the "triplet" in these circumstances was due to the presence of non-enriched CO_2-adduct. The ratios of the centre line to the sum of the outer lines of the "triplet" could thus be used as a measure of the degree of isotopic enrichment in the carbon dioxide used for the trapping reaction.



(108)



(122)

The analogous ^{13}C labelled CO_2-adduct (122; R = Me, R' = Ph) prepared from dimethyl phenylphosphonite had a ^{31}P n.m.r. chemical shift of δ_P -37.0 p.p.m. and was also observed as a small doublet ($J_{PC} \sim 10$ Hz). The ^{13}C n.m.r. spectra of these labelled compounds were also studied. As expected the labelled site was clearly visible even without signal accumulation. For the CO_2-adduct (122; R = Me, R' = Ph) the signal at δ_C 158.47 p.p.m. was clearly labelled and showed the same J_{PC} coupling as observed in the ^{31}P n.m.r. spectrum. Although the ^{13}C n.m.r. signal at 158.47 p.p.m. was in the region of the spectrum characteristic of ester carbonyls, the proton-coupled spectrum showed no sign of the long range proton-carbon coupling which we would expect to observe on the carbonyl carbon of a methyl ester. This is entirely consistent with the proposed site of ^{13}C incorporation, the carbonyl carbon of the carboxyl group. Irradiation at δ_P -37.05 p.p.m. in the ^{31}P n.m.r. spectrum caused the signal at 158.47 p.p.m. in the ^{13}C n.m.r. spectrum to collapse to a singlet, confirming that the doublet character of the ^{13}C n.m.r. signal arose from coupling to the phosphorus atom in the CO_2-adduct (108; R = Me) (Plate 15).

The incorporation of the carbon dioxide into the CO_2-adducts (108; R = Me) and (122; R = Me, R' = Ph) thus appeared to have proceeded as expected.

The efficiency of the CO_2-trapping reaction had also been clearly demonstrated. This poses the question, why should carbon dioxide show such a high reactivity towards the 1:1 intermediates (87; R = alkyl), (135; R = Ph, R' = OMe or OEt) and (135; R = OMe, R' = Ph) formed in the reaction of the trivalent phosphorus compound and dimethyl acetylenedicarboxylate? The most likely explanation

^{13}C N.m.r. spectra of 5[^{13}C]-2,2-dimethoxy-3,4-bis(methoxycarbonyl)-5-oxo-2-phenyl-Δ^3-oxaphospholene (122; R = Ph, R' = OMe, 5[^{13}C]). Single pulse experiments.

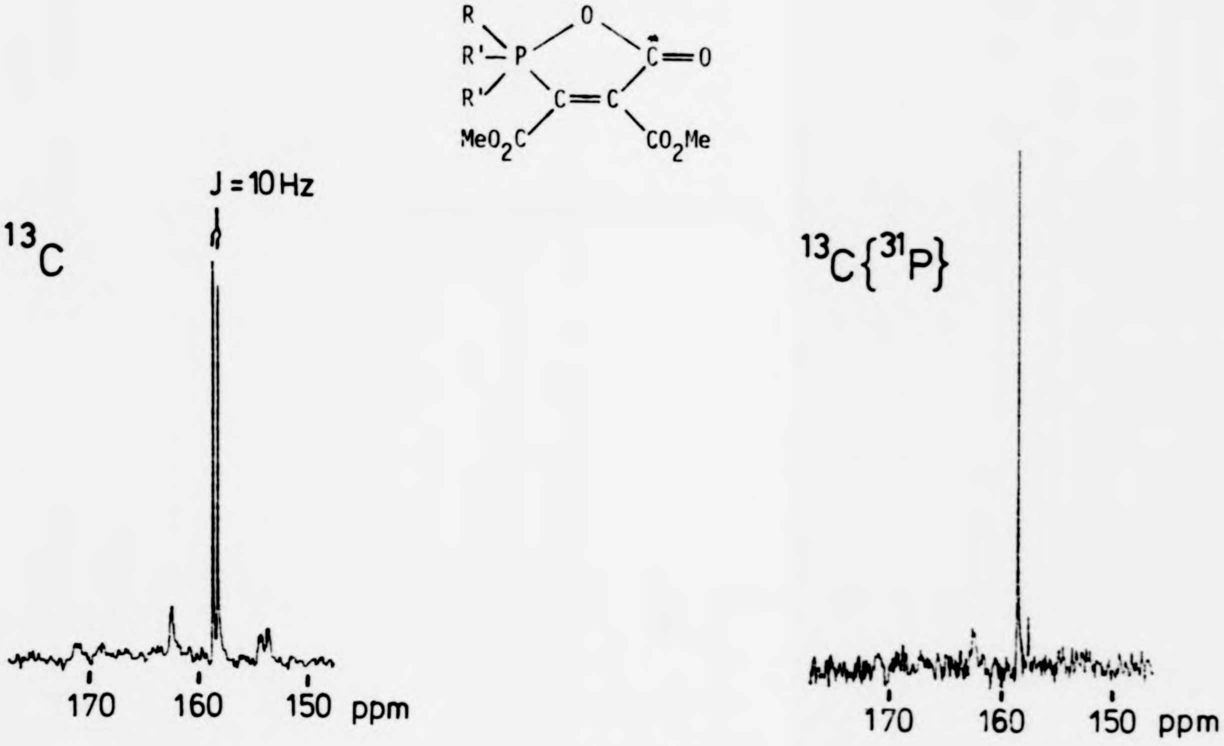
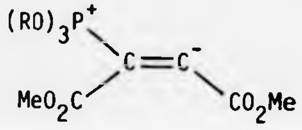
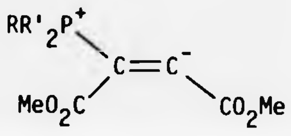


Plate 15

is that there is some initial interaction between the phosphorus centre in the 1:1 intermediates (87) and (135), and one of the oxygen atoms in the carbon dioxide. Such an interaction would lead to an increased polarity in the carbon-oxygen bond which in turn would increase the electron deficiency at the carbon. This centre would then be a more attractive site for nucleophilic attack and hence account for the enhanced reactivity of the carbon dioxide towards the 1:1 intermediates (87) and (135).



(87; R = alkyl)



(135; R = Ph, R' = OEt, OMe
R = OMe, R' = Ph)

7. AN INVESTIGATION INTO THE SITE OF INCORPORATION OF ^{13}C ENRICHED CARBON DIOXIDE IN THE FURAN (131) AND ITS YLIDE PRECURSOR.

Although the incorporation of the ^{13}C enriched carbon dioxide into the CO_2-adduct (108; R = Me) had proceeded as expected, the site of incorporation in the furan (131; R = Me) and its ylide precursor were quite unexpected.

The ^{13}C labelled ylide, initially proposed as having the structure (124), prepared from trimethyl phosphite and dimethyl acetylenedicarboxylate in the presence of ^{13}C labelled carbon dioxide, was observed as a doublet (J_{PC} 21 Hz) at δ_P 47.4 p.p.m. in the ^{31}P n.m.r. spectrum. However, there appeared to be a rather lower degree of labelling than expected, since the centre line corresponding to the unlabelled ylide was greater than 50% of the total signal (Plate 16).

^{31}P N.m.r. proton decoupled spectrum of the ylide at δ_P 47.44 p.p.m. prepared using ^{13}C-enriched carbon dioxide. Single pulse experiment.

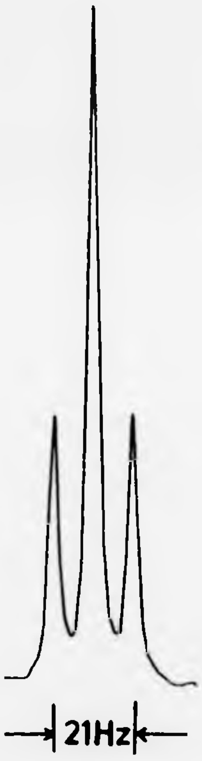
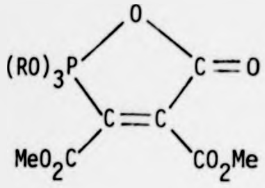
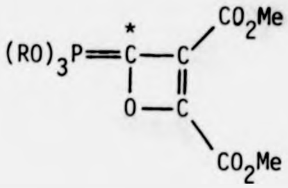


Plate 16

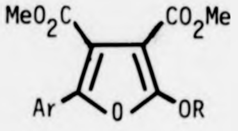
Similarly, the corresponding ylide prepared from dimethyl phenylphosphonite was observed as a doublet at δ_P 65.3 p.p.m. (J_{PC} 19 Hz), again with a reasonably intense centre line apparently due to non-labelled ylide.



(108)



(124)



(131)

From the originally proposed structure (124) we would have expected incorporation of the carbon dioxide to be such that the labelled carbon would be adjacent to the phosphorus, as indicated by the asterisk. This was clearly not the case since this latter situation would have given rise to a ^{31}P n.m.r. signal showing a J_{PC} coupling of 250 Hz (see Table 25).

The ^{13}C n.m.r. spectra of the labelled ylides were even more surprising. As well as the doublet showing coupling to phosphorus as indicated by the ^{31}P n.m.r. spectra, there was also a second labelled signal, showing no coupling to phosphorus. These two labelled signals, which were both in the ester carbonyl region of the spectrum, were of equal intensity and both showed long range coupling to ester methyl protons in the proton-coupled ^{13}C n.m.r. spectra. For the ylide prepared from trimethyl phosphite the signals were at δ_C 163.45; d, J_{PC} 21 Hz and 154.52 p.p.m. (Plate 17) while for the ylide prepared from dimethyl phenylphosphonite the signals were at δ_C 162.48, d, J_{PC} 19 Hz and 154.03 p.p.m. This clearly indicated that scrambling of the label between two sites had occurred on conversion of the

^{13}C N.m.r. spectrum of the ylide at δ_P 47.44 p.p.m. prepared using ^{13}C-enriched carbon dioxide (proton decoupled). Single pulse experiment.

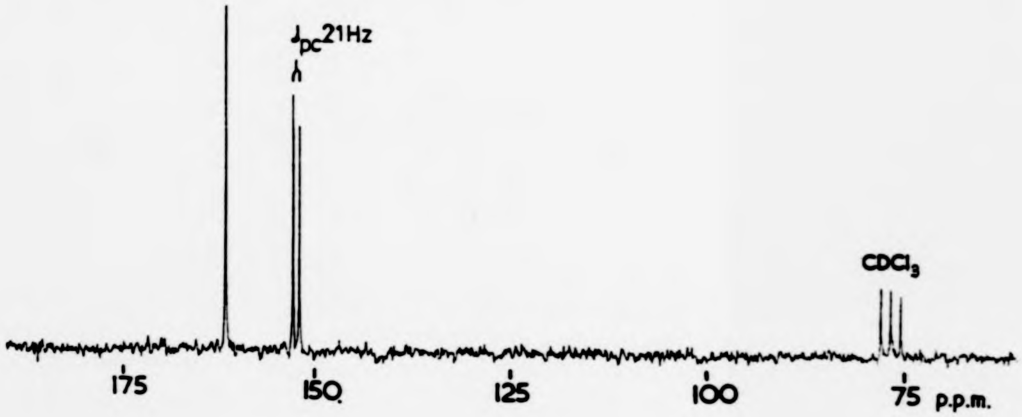
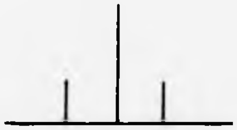


Plate 17

CO_2-adducts to the ylides. However, it was not easy to explain how these labels had apparently become located in the carbonyl carbons of what appeared to be two ester functions.

Under these circumstances it was of importance to establish those carbon atoms which were adjacent to the sites of ^{13}C incorporation. Fortunately, as previously discussed, the presence of the ^{13}C label would be expected to give rise to a splitting of the ^{13}C n.m.r. signals of adjacent carbons due to J_{CC} coupling [see Introduction]. Since the level of ^{13}C incorporation was only about 45% at each site of incorporation, about 55% of the signal intensity of the natural abundance signals would be unaffected by coupling. We therefore expected to observe the signals showing coupling to the ^{13}C labelled site as distorted triplets (see Fig. 31). Coupling to phosphorus would, of course, further complicate the appearance of the signals (see Fig. 31).



$^1J_{CC}$ coupling to a single carbon atom from an adjacent carbon atom having about 45% ^{13}C enrichment.

Introduction of J_{PC} coupling.

Fig. 31

The ^{13}C n.m.r. spectrum of the labelled ylides (108; R = Me) and (122; R = Ph, R' = OMe) were therefore determined using "block averaging" techniques so that signals from the non-enriched sites could be clearly observed despite the presence of the large signals resulting from the sites of isotopic enrichment (see Plate 18).

Rather surprisingly only one carbon signal showed the expected coupling to the ^{13}C labels. Moreover, after phosphorus decoupling this signal was observed as a "doublet" with the expected intense central line of the anticipated "triplet" having only modest intensity. For the ylide prepared by trimethyl phosphite the "doublet" was observed at δ_C 86.09 p.p.m., J_{CC} 90 Hz. In the presence of the coupling to phosphorus an additional J_{PC} coupling of 19 Hz was also observed.

The only explanation for the "doublet" character of the signal at δ_C 86.09 p.p.m. was that the carbon giving rise to 'this' signal was adjacent to both sites of ^{13}C incorporation. Furthermore, since only one carbon exhibited coupling to the isotopically labelled sites we must conclude that only one carbon atom is adjacent to the labelled sites. We therefore appear to have a fragment such as that shown in Fig. 32 in the labelled ylide.

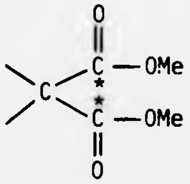


Fig. 32

However, at the same time we must remember that the two labelled sites have significantly different ^{13}C n.m.r. shifts and that one of the signals shows coupling while the other does not.

^{13}C N.m.r. spectra of the ylide at δ_P 47.44 p.p.m. prepared using ^{13}C-enriched carbon dioxide with 'block averaging'. Multiple pulse experiment.

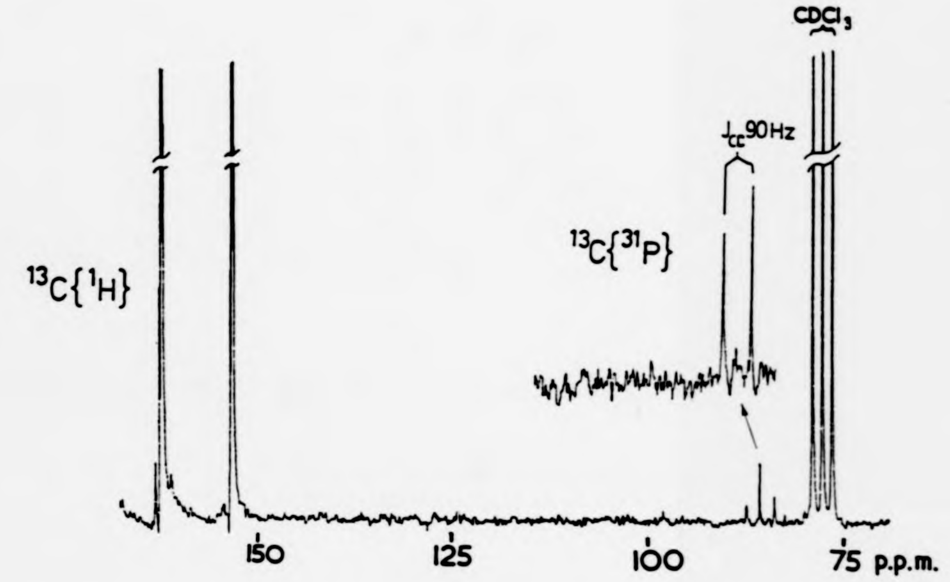
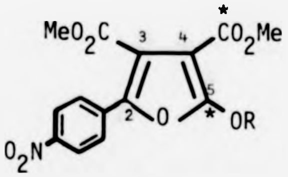


Plate 18

In addition, the ^{13}C n.m.r. shift of the carbon adjacent to the sites of labelling is at reasonably low field for an sp^3 carbon.

Bearing in mind the fact that we have already identified the presence of an ylidic carbon attached to a phosphorus having three methoxy groups, we are left with only one carbon and one oxygen atom unaccounted for in the structure of this ylide. Furthermore, ^{13}C n.m.r. spectrum showed the absence of any ketone group. Since no satisfactory structure could be proposed on the basis of these assumptions it was decided to extend the ^{13}C-labelling study to the formation of the furan (131; R = Me). Since the structure of this material had been established beyond any doubt it was of interest to see the location of ^{13}C-enrichment in this material.



(131; R = Me)

As with the ylide from trimethyl phosphite, previously discussed, the ^{13}C n.m.r. spectrum of the labelled furan (131; R = Me) showed two sites of labelling. Both signals were again in the carbonyl region of the spectrum, and both showed long range coupling to methyl groups in the proton-coupled ^{13}C n.m.r. spectrum. In addition, only one natural abundance ^{13}C signal showed coupling to the sites of labelling. This was clearly identified as C-4 in (131; R = Me), that resonating at δ_C 93.14 p.p.m. This was observed to have doublet character (J_{CC} 90 Hz) indicating that it was adjacent to both sites of labelling [see earlier Discussion]. This would therefore indicate that the sites of labelling are C-5 and the ester carbonyl at C-4, rather than the two ester carbonyls at C-3 and C-4.

Since the effects of labelling were similar in both the furan (131; R = Me) and the ylide precursor this suggested that the fragment containing the labelling in the ylide might be that shown in Fig. 33 rather than that previously indicated in structure (124).

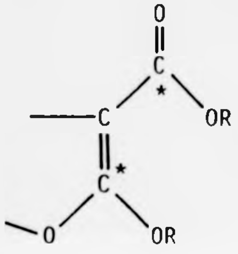
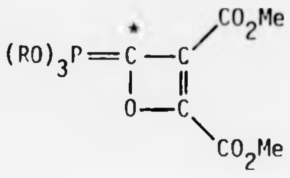
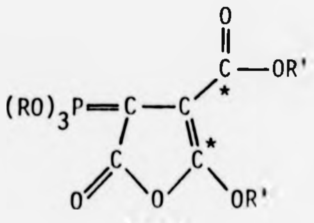


Fig. 33



(124)

Such a structure would explain the difference in ^{13}C n.m.r. chemical shifts and coupling to phosphorus observed for the labelled signals in the ylidic precursor of the furan (131; R = Me). This in turn would suggest that the structure of the ylide prepared from trimethyl phosphite and dimethyl acetylenedicarboxylate in the presence of carbon dioxide is (136; R,R' = Me) 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane. As we will see in later discussion, this structure satisfactorily accounts for the chemical behaviour of the ylide.



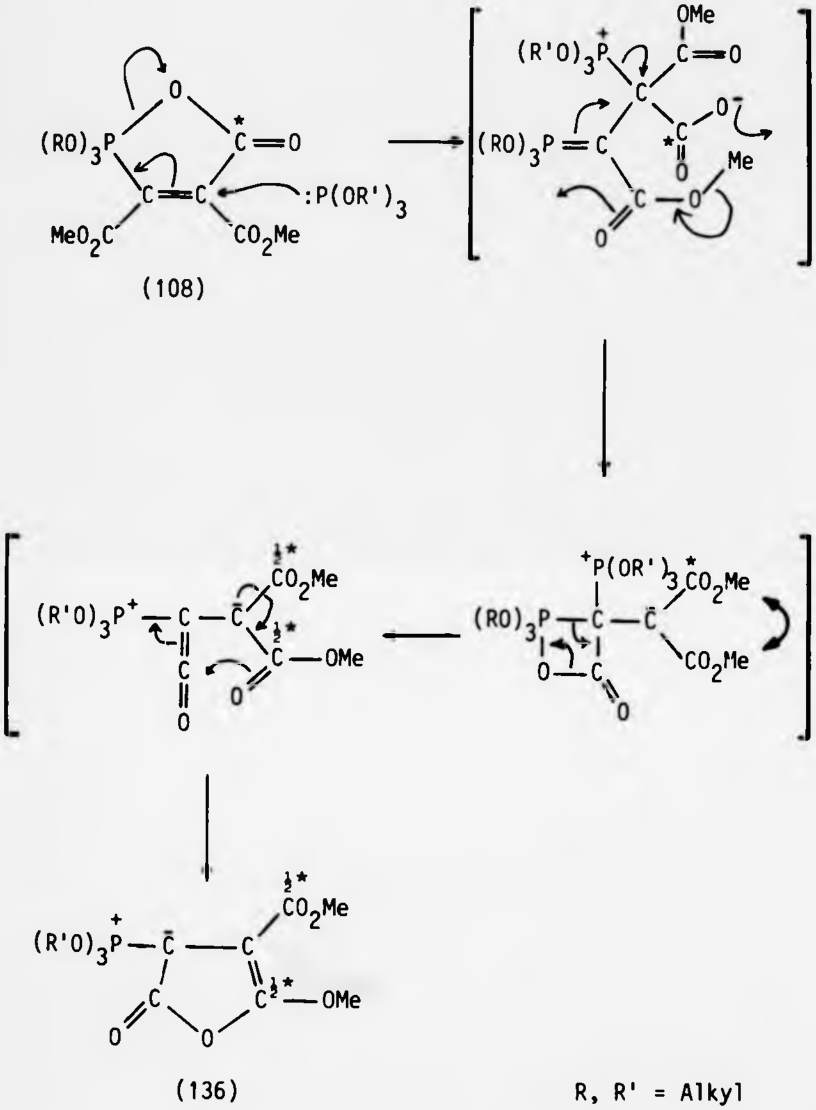
(136)

* Position of ^{13}C enrichment.

It is also clear that the formation of the ylide (136) from its precursor, the CO_2-adduct (108), involves a number of steps. A possible mechanism is shown in Fig. 34. This mechanism accounts for the expulsion of the molecule of trimethyl phosphate from the original CO_2-adduct (108) and explains how the scrambling of the ^{13}C label between two sites occurs.

The nucleophilic attack of an additional molecule of trivalent phosphorus compound on the CO_2-adduct (108) leads to the formation of a free carboxylate function. This free carboxylate function is derived from the ^{13}C enriched carbon dioxide incorporated into the CO_2-adduct (108), and indicated by the asterisk (*). The proposed mechanism then provides for the subsequent alkylation of the free carboxylate function. This results in the presence of two methoxycarbonyl groups, one of which has a ^{13}C enriched carbonyl, and both attached to a central carbon atom. The equilibration of the two methoxycarbonyl groups about the central carbon atom then results in the position of ^{13}C enrichment becoming equally distributed between two sites. This is indicated by (½*) in Fig. 34. The cyclisation to form the ylide (136) thus results in two sites of ^{13}C enrichment both attached to the same central carbon atom.

The ^{31}P n.m.r. spectral data for a number of ylides prepared from the CO_2-adducts (108; R = alkyl) is given in Table 30. The structure of the ylide (136) is clearly supported by the ^{13}C n.m.r. spectral data obtained (Table 31). The ^{13}C n.m.r. spectrum of the ylide (136; R, R' = Me) is given in Plate 19.



Site of ^{13}C enrichment from ^{13}C enriched carbon dioxide indicated by (*).

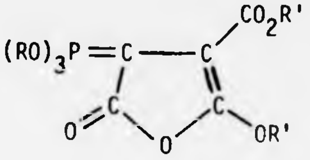
Fig. 34

TABLE 30

^{31}P N.m.r. spectral data.

5-Alkoxy 4-alkoxycarbonyl-2,3-dihydro-3-furanylidenetrialkoxyphosphoranes

(136).



R	R'	$\delta^{a,b}$
Me	Me	47.44
Et	Et	40.49
Et	Me	40.16
Pr^i	Me	40.34^c

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference.

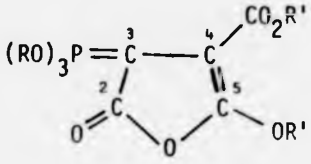
[b] [^{2}H]Chloroform, 26 °C.

[c] [^{2}H$_8$]Toluene, 26 °C.

TABLE 31

^{13}C N.m.r. spectral data.

5-Alkoxy 4-alkoxycarbonyl-2,3-dihydro-3-furanylidenetrialkoxyphosphorane (136).



(136)

δ[a]		R,R'=Me[b]	R=Et, R'=Me[c]	R,R'=Et[c]
	R'	50.80	50.27	13.50
		56.97	56.65	14.08
				58.67
				65.91
	R	55.79(7)	15.05(7)	13.08
			65.01(6)	64.86(6)
	C-3	47.88(251)	48.85(249)	48.56(244)
	C-4	85.36(15)	84.08(15)	85.32(15)
	C-5	163.41	162.36	161.97
	C=O	154.33(21)	153.20(21)	152.86(21)
		163.31(27)	163.24(24)	163.46(26)

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses.

[b] [$^2H_8$]Toluene, -30 °C.

[c] [^{2}H]Chloroform, -30 °C.

^{13}C N.m.r. spectrum of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me) (proton decoupled).

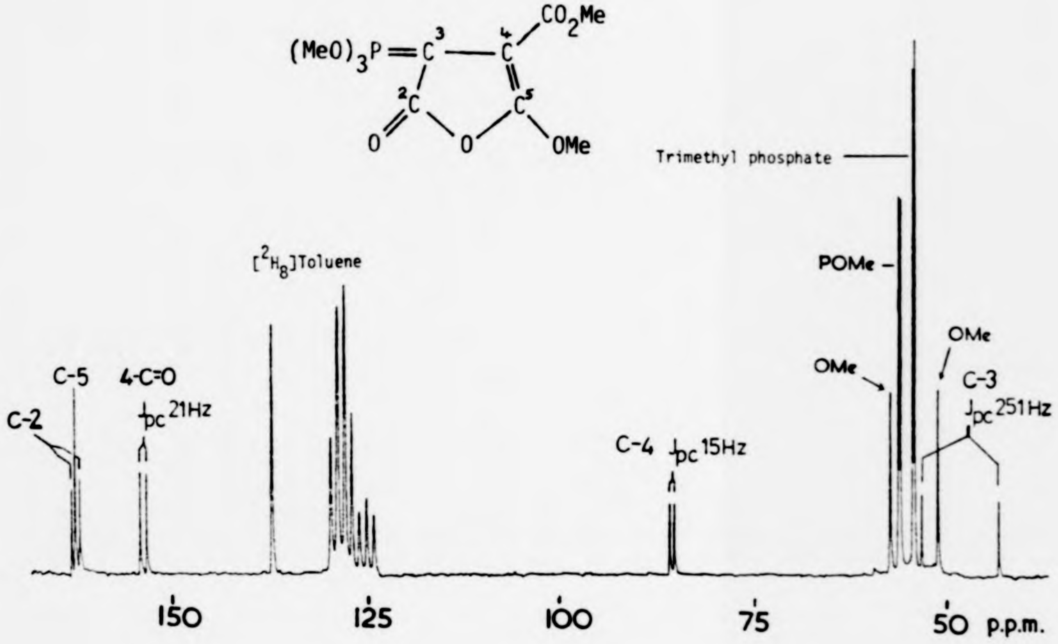
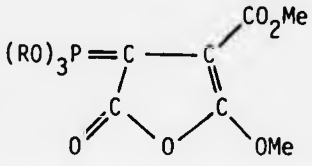


Plate 19

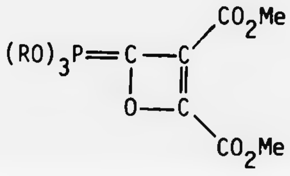
B. *Investigation of some reactions of the ylide formed from the reaction of trialkyl phosphites with dimethyl acetylenedicarboxylate in the presence of carbon dioxide.*

1. REACTION OF THE YLIDE WITH ALCOHOL.

As previously discussed it was the reaction of the ylide (136) with alcohol which first alerted us to the unsatisfactory nature of the originally proposed structure (124).



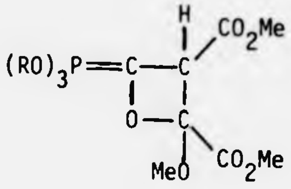
(136)



(124)

Thus, the treatment of the ylide (136; R = Me) with one equivalent of methanol led to the formation of two components, as shown by the ^{31}P n.m.r. spectrum of the reaction mixture. The proton-coupled ^{31}P n.m.r. spectrum of these two components showed that in both components three alkoxy groups were still attached to the phosphorus, and this together with their ^{31}P n.m.r. shifts at δ_P 60.4 and 58.5 p.p.m. suggested that these components were both ylides. This was supported by the ^{13}C n.m.r. spectra of these components [see later Discussion] which showed the carbons directly attached to the phosphorus atoms to exhibit the large values of $^1J_{PC}$ which we have found to be characteristic of other such ylides we have studied. More importantly, these ylides were reasonably stable in the presence of additional methanol, indicating that these systems were clearly stabilised ylides. The addition of methanol to the ylide (124; R = alkyl) would have had to lead to the formation of a structure such as

(137; R = alkyl) if the ylide character of this material was to have been maintained. However, this structure (137; R = alkyl) could not account for the observed stability of this ylide in the presence of methanol.

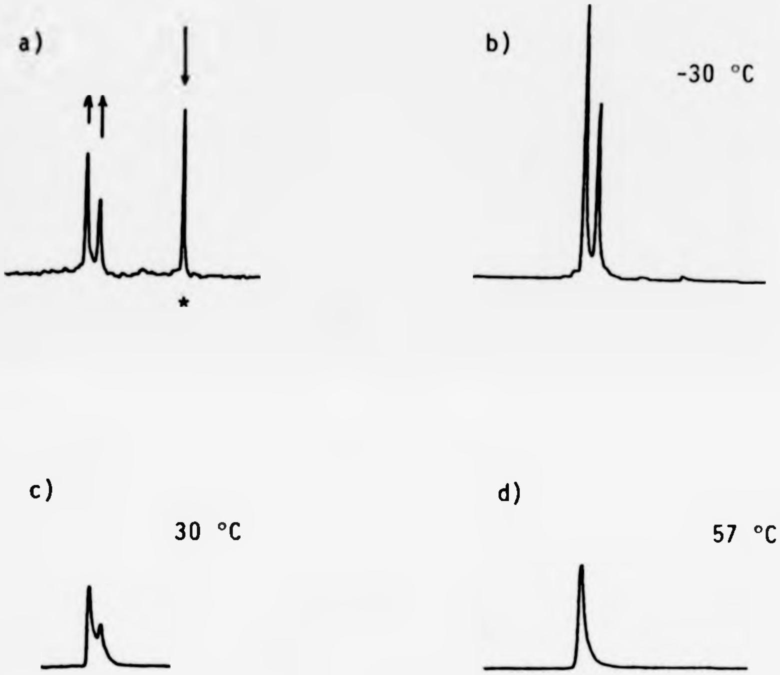


(137)

Interestingly, the ^{31}P n.m.r. resonance signals for both stabilised ylides showed some broadening at room temperature, suggesting that they might be involved in some equilibrium process. This was confirmed by warming the sample of the ylides to 57 °C, whereupon the two ^{31}P n.m.r. signals broadened and then coalesced (Plate 20). Attempts to isolate the stabilised ylides by chromatography on silica or alumina, or treatment of the ylides with hydrogen chloride both led to the formation of a single phosphorus-containing component at δ_P 21.2 p.p.m. As expected this was shown to be due to protonation of the ylides and subsequent dealkylation of the quasi-phosphonium salts to give a phosphonate. Thus, the loss of the methoxy group from the phosphorus was clearly shown by the doublet of septet character observed for the phosphonate derived from the stabilised ylides prepared from treatment of ylide, (136; R = Me) with ethanol.

In the ^{13}C n.m.r. spectrum of the phosphonate the carbon adjacent to the phosphorus was readily identified as the doublet at δ_C 44.4 p.p.m. ($^{1}J_{PC}$ 130 Hz). Each half of the doublet was split

Temperature dependence of the ^{31}P n.m.r. (proton decoupled) spectrum of the ylide produced on treatment of phosphorane (136, R,R' = Me) with methanol.



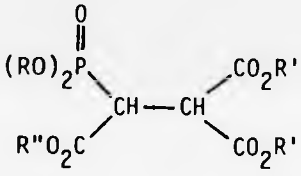
a) Addition of alcohol to the ylide (*) (136) produces two new components in the ^{31}P n.m.r. spectrum, b).

c) Warming of the components in the n.m.r. probe causes signal broadening.

d) Further warming to 57 °C causes coalescence of the two signals in the ^{31}P n.m.r. spectrum.

Plate 20

into a doublet of doublets in the proton-coupled ^{13}C n.m.r. spectrum clearly indicating that not only was this α-carbon protonated but there was also a proton present on the β-carbon. This enabled the β-carbon to be assigned as the singlet at δ_C 50.16 p.p.m. which was also split into a doublet of doublets in the proton-coupled spectrum. The remaining ^{13}C n.m.r. data suggested that there were also three carboxylic ester groups present in the molecule. This therefore suggested that the phosphonate which had been produced was (138; R,R',R" = Me) (Table 32) (Plate 21).



(138)

In order to confirm this an independent synthesis of this material was carried out.

2. SYNTHESIS OF DIMETHYL 1,2,2-TRIS(METHOXYCARBONYL)ETHYL-PHOSPHONATE.

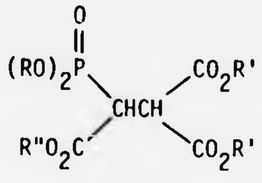
The route chosen for the synthesis of phosphonate (138, R,R',R" = Me) is given in Fig. 35. The malonic ester was commercially available and the trialkyl phosphonoacetate was readily prepared by the Michaelis-Arbusov reaction of trimethyl phosphite with the appropriate chloroacetate.

Two methods were investigated for the formation of the desired phosphonate (138; R,R'R" = Me) from the active methylene precursor.

TABLE 32

N.m.r. spectral data.

Dimethyl 1,2,2-Tris(methoxycarbonyl)ethylphosphonate (138; R,R',R" = Me).



(138)

$\delta(^{13}C)^a$	R,R',R" = Me
R	53.59(6)
	53.68(6)
R'	53.16
	53.16
R"	52.98
α-C	44.40(131)^b
β-C	50.16^c
C=O	166.81
	167.00(16)
	167.56
$\delta(^{31}P)^d$	21.2

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] Multiplicity and J_{CH} from proton-coupled spectrum: d,d; 142, 7 Hz.

[c] Multiplicity and J_{CH} from proton-coupled spectrum: d,d; 135, 5 Hz.

[d] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; [^{2}H]Chloroform, 26 °C.

^{13}C N.m.r. spectrum of dimethyl 1,2,2-tris(methoxycarbonyl)ethylphosphonate

(138; R,R',R" = Me) (proton decoupled).

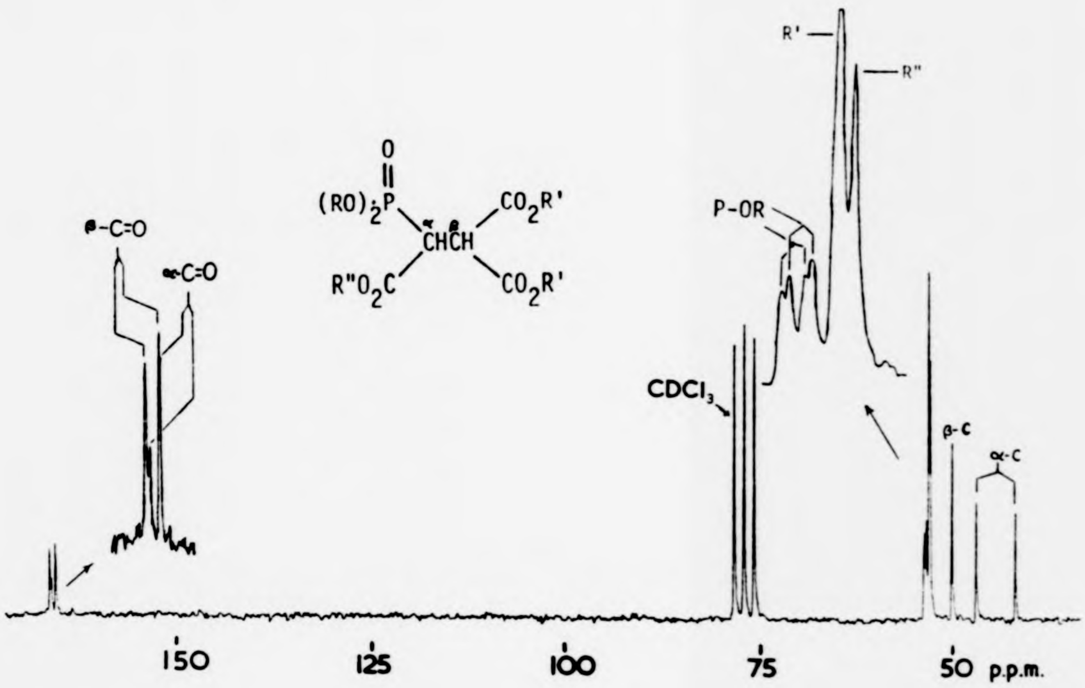


Plate 21

In the first, the phosphonate (139) was converted to its bromo derivative (140) and then reacted with the sodium salt of dimethyl malonate (141). In the second, the bromo derivative of dimethyl malonate was reacted with the anion from the phosphonate (139). In both cases problems arose due to the preferential formation of the tetraalkyl ethane-1,1,2,2-tetracarboxylate. Considerable efforts were therefore made to reduce this undesirable side-reaction but with only modest success. The best method for the formation of the desired phosphonate (138; R,R',R" = Me) involved the slow controlled addition of a freshly prepared solution of the anion of the malonic ester (141) to a freshly prepared sample of the bromophosphonate (140), while maintaining the temperature at 20 °C. A small quantity (about 10%) of the desired phosphonate (138; R,R',R" = Me) was isolated from the resulting reaction mixture by preparative layer chromatography and shown to be identical spectroscopically to the product formed via the carbon dioxide route. This therefore confirmed that reaction of the ylide (136; R = Me) with methanol followed by treatment with hydrogen chloride led to the formation of the phosphonate (138; R,R',R" = Me).

It is again of interest to contrast the relative ease of formation of the phosphonates (138) via the carbon dioxide route, with that via the malonate ester. In the former, yields in the order of 80% were often achieved while in the latter only a few percent were observed. The ^{31}P and ^{13}C n.m.r. spectral data for a number of phosphonates (138) prepared via the carbon dioxide route is given in Tables 33 and 34 respectively.

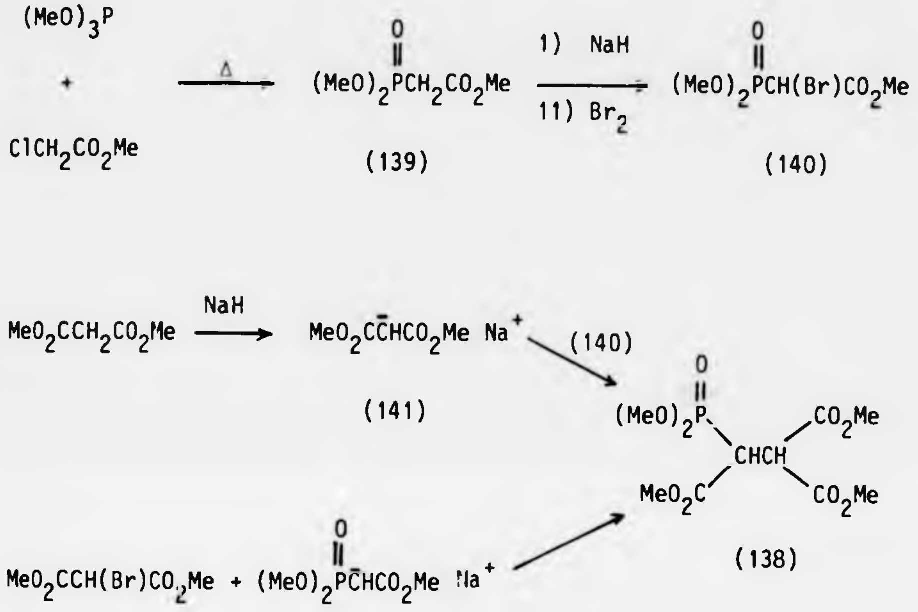
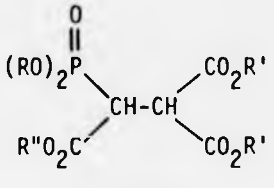

(MeO)3P
+
ClCH2CO2Me
Δ
(MeO)2P(O)CH2CO2Me
(139)
1) NaH
11) Br2
(MeO)2P(O)CH(Br)CO2Me
(140)
MeO2CCH2CO2Me
NaH
MeO2CC̄HCO2Me Na+
(141)
(140)
(MeO)2P(O)
CHCH
CO2Me
MeO2C
CO2Me
(138)
MeO2CCH(Br)CO2Me + (MeO)2P(O)C̄HCO2Me Na+

Fig. 35

TABLE 33

^{31}P N.m.r. spectral data.

Dialkyl 1,2,2-Tris(alkoxycarbonyl)ethylphosphonate (138).



(138)

R	R'	R"	δ[a]
Me	Me	Me	20.9[b], 21.2[c]
Me	Me	Et	21.34[c] (d of sept).
Et	Me	Et	18.54[b] (d of quintets; 22, 8).
Et	Et	Et	18.64[b,c] (d of quintets; 22, 8).

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference; J_{PH} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

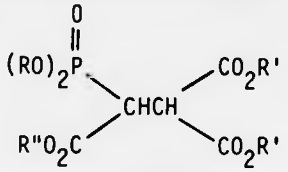
[b] Using deuteriated alcohol, R"OD. [(143), see later Discussion].

[c] Using alcohol, R"OH.

TABLE 34

^{13}C N.m.r. spectral data

Diethyl 1,2,2-Tris(ethoxycarbonyl)ethylphosphonate (138; R,R',R" = Et).



(138)

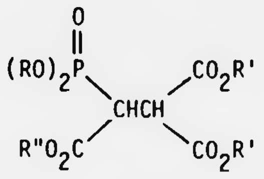
δ^{a}	R,R',R" = Et
R	16.25(6)
	63.11(6)
R'	13.93
	61.97
R"	13.93
	62.06
α-C	45.11(130)
β-C	50.82
C=O	166.45(5)
	166.82(22)
	167.13(13)

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

TABLE 34 continued

^{13}C N.m.r. spectral data

Dialkyl 1,2,2-Tris(alkoxycarbonyl)ethylphosphonate (138).



(138)

δ[a]	R,R" = Et; R' = Me	R,R' = Me; R" = Et
R	16.22(6)	53.58(5)
	63.23(6)	
R'	52.72	52.91
		53.08
R"	13.89	13.88
	62.15(3)	62.24(4)
α-C	45.0(130)	44.41(130)[b]
β-C	50.58	50.46[b]
C=O	166.92(3)	c
	167.50(18)	166.62(18)
	167.64(5)	c

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] Multiplicity from ^{13}C n.m.r. Off-resonance proton-coupled spectrum, d of d.

[c] Multiple signals.

3. MECHANISM FOR THE FORMATION OF THE PHOSPHONATES (138) FROM THE ORIGINAL YLIDE PRECURSOR.

Having established the structure of the ylide (136) by ^{13}C labelling studies it was feasible to rationalise its reaction with alcohol which eventually led to the formation of the phosphonate (138).

The observed reaction of the ylide (136) with alcohol can be explained by the mechanism proposed in Fig. 36.

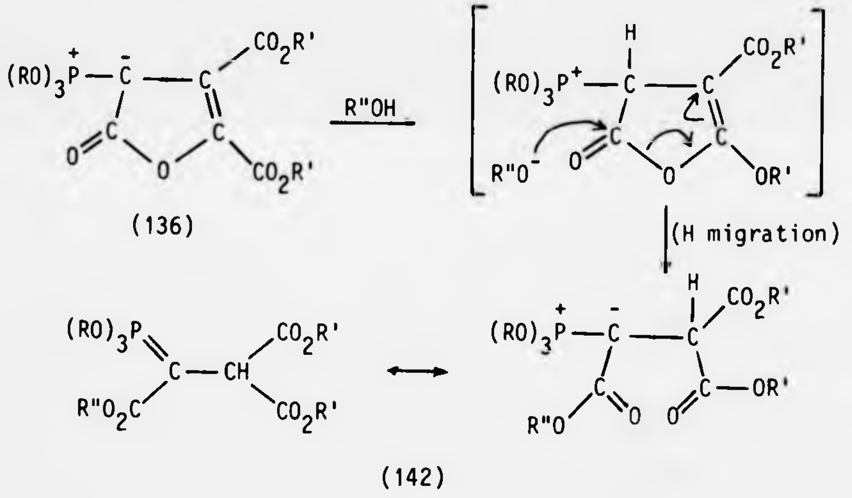
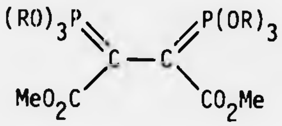


Fig. 36

Although protonation probably initially occurs at the α-carbon of the ylide (136), it can be seen that subsequent ring opening by the alkoxide ion leads to the formation of an anion <u>beta</u> to the phosphonium centre. The migration of the proton from the α-carbon to the β-carbon then moves the anionic site adjacent to the phosphonium centre where stabilisation can be more effectively achieved.

The initially formed ylides can thus be seen to have the structure (142). The presence of the two signals in the ^{31}P n.m.r. spectrum which are in equilibrium with each other can now be seen to be due to restricted rotation about the alkoxycarbonyl group on the *α*-carbon. This phenomenon is clearly visible in the ^{31}P and ^{13}C n.m.r. spectra (Tables 35 and 36) of the stabilised ylides (142). We have observed a similar temperature dependent ^{31}P n.m.r. spectrum in other ylides containing an α-alkoxycarbonyl group such as the 1,2-diphosphoranes (88) [see earlier Discussion].



(88; R = alkyl)

The presence of the α-alkoxycarbonyl group would also confer a high degree of stability on the ylide, thus accounting for its stability in the presence of excess alcohol. This enhanced stability also accounts for our observations that the ylide (142) was unreactive towards a number of aldehydes, including 4-nitrobenzaldehyde. With this latter aldehyde no reaction with the ylide (142) was observed even after heating under reflux in toluene for over 18 h.

A sample of ^{13}C labelled ylide (142) was also prepared from ^{13}C-enriched carbon dioxide, and as predicted, the sites of labelling were as indicated in Fig. 37, the β-carbonyl carbon atoms.

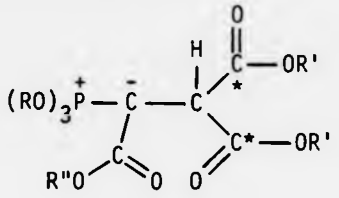
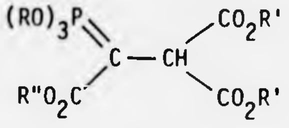


Fig. 37

TABLE 35

^{31}P N.m.r. spectral data

1,2,2-Tris(alkoxycarbonyl)ethylidenetrialkoxyphosphorane (142).



(142)

R	R'	R"	δ^a		
Me	Me	Me	60.37	$58.48^{b,c,d}$	(1)
Me	Me	Et	59.42	$57.46^{b,c}$	(2)
Me	Me	Et	59.32	$57.62^{d,e}$	
Et	Me	Me	53.07	$51.14^{c,e}$	
Et	Me	Et	53.69	$51.90^{c,d,e}$	(3)
Et	Et	Et	53.15	$51.77^{b,c}$	

[a] Shifts in p.p.m. from 85% phosphoric acid; positive shifts to low field of reference.

[b] [^{2}H]Chloroform, 26 °C.

[c] Prepared using non-deuteriated alcohol, R"OH.

[d] Prepared using deuteriated alcohol, R"OD.

[e] [$^2H_8$]Toluene, 26 °C.

(1) Multiplicity from proton-coupled spectrum, dec.

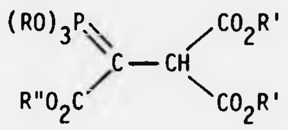
(2) Multiplicity and coupling from proton-coupled spectrum; d of dec, J_{PH} 6, 12 Hz.

(3) Multiplicity and coupling from proton-coupled spectrum, d of sept, J_{PH}7 Hz.

TABLE 36

^{13}C N.m.r. spectral data.

1-Ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142).



(142)

δ^a	R,R' = Me; R" = Et^b	
	Major isomer^c	Minor isomer^c
R	54.58(5)	54.71(5)
R'	50.41	
	52.23	
R"	14.10	
	61.13	
α-C	39.96(231)	41.54(236)
β-C	49.99	50.09
α-C=O	169.80(19)	d
β-C=O	171.19	171.06
β-C=O	171.87	171.59

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses.

[b] [^{2}H]Chloroform, -15 °C.

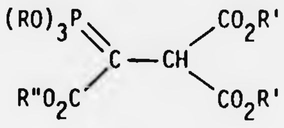
[c] Isomerism due to restricted rotation about the bond to the α-alkoxycarbonyl group.

[d] Minor isomer obscured.

TABLE 36 continued

^{13}C N.m.r. spectral data.

1,2,2-Tris(alkoxycarbonyl)ethylidenetrialkoxyphosphorane (142).



(142)

δ[a]	R,R' = Me; R" = Et[b]		R,R',R" = Et[c]	
	Major Isomer[d]	Minor Isomer[d]	Major Isomer[d]	Minor Isomer[d]
R	54.50(5)	54.61(5)	14.13[e] 64.01(5)	
R'	50.24 51.84		15.86[e] 57.17	
R"	14.15 61.03		15.07[e] 60.94	
α-C	39.71(232)	41.66(235)	41.04(230)	42.29(234)
β-C	49.87	49.97	50.12[f]	50.48
α-C=O	169.39(20)	169.60(25)	169.85(19)	
β-C=O	171.41	171.02	171.48	171.24
β-C=O	172.06	171.70	171.48	171.24

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses.

[b] [$^2H_8$]Toluene, -30 °C.

[c] [^{2}H]Chloroform, -30 °C.

[d] Isomerism arising due to restricted rotation about the bond to the α-alkoxycarbonyl group.

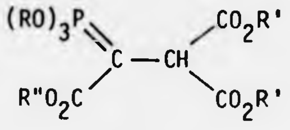
[e] Tentative assignment, signals obscured by impurities.

[f] Prepared using deuteriated ethanol (EtOD); β-C deuteriated at δ_P 50.22 p.p.m. broadened.

TABLE 36 continued

^{13}C N.m.r. spectral data.

1-Ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142).



(142)

δ[a]	R,R" = Et; R' = Me[b]		R,R" = Et; R' = Me[c]	
	Major isomer[d]	Minor isomer[d]	Major isomer[d]	Minor isomer[d]
R	16.41	15.88	16.39	15.88
	63.97(5)	64.35(5)	63.89(4)	64.37(5)
R'	49.80		49.97	
	51.79		51.89	
R"	14.20		14.20	
	60.89		60.99	
α-C	40.24(231)	41.81(234)	40.12(231)	41.68(233)
β-C	49.63[e]		50.10	
α-C=O	169.27(20)	169.24(25)	169.31(18)	168.63[e]
β-C=O	171.50	171.09	171.62	171.24
β-C=O	172.11	171.72	172.21	171.87

[a] Shifts in p.p.m. from Me$_4$Si; J_{PC} in Hz in parentheses.

[b] [^{2}H$_8$]Toluene, -30 °C.

[c] [^{2}H$_8$]Toluene, -50 °C.

[d] Isomerism arising due to restricted rotation about the bond to the α-alkoxycarbonyl group.

[e] Broadened signal.

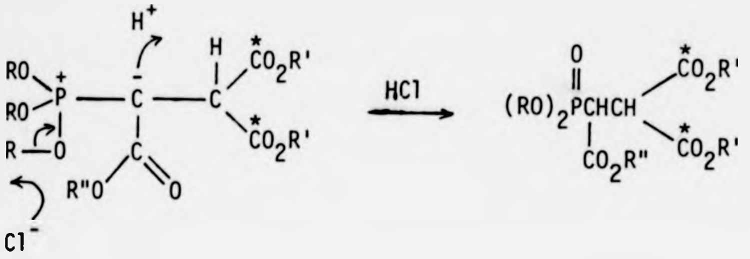
(143; R,R',R" = Et). In this latter system the β-carbon signal was clearly observable as a triplet at δ_C 50.46 p.p.m. t, $^3J_{CD}$ 21 Hz, and this aided the identification of the β-carbon signal in analogous compounds. Thus, the δ-carbon signal was for (143; R,R',R" = Me) at δ_C 49.90 p.p.m., t, $^3J_{CD}$ 21 Hz, and for (143; R,R" = Et, R' = Me) at δ_C 50.58 p.p.m. (signal broadened).

4. REACTION OF THE YLIDE (136) WITH CARBONYL COMPOUNDS.

The reaction of the ylide (136) with 4-nitrobenzaldehyde has already been discussed during our consideration of the structure of the ylide (136). To summarise, it was found that heating a sample of the ylide (136; R = Me) with 4-nitrobenzaldehyde in toluene led to a reaction in which the ^{31}P n.m.r. signal from the ylide (136) was gradually replaced by two signals at δ_P 140 and 21.3 p.p.m. The signal at δ_P 140 p.p.m. was readily identified as trimethyl phosphite, while that at δ_P 21.3 p.p.m. appeared to be a phosphonate. In addition, the furan (131; R = Me) was produced in good yield as a yellow crystalline compound. This behaviour is clearly not consistent with the expected Wittig-type reaction which might have been predicted for the reaction of an ylide with an aldehyde.

A proposed mechanism for the formation of the furan (131; R = Me) is given in Fig. 39. The mechanism is consistent with the observed sites of incorporation of the ^{13}C-enriched carbon dioxide and also explains how the alkoxy group at C-5 is derived. The formation of the stable furan ring system also helps explain the observed expulsion of trimethyl phosphite (itself a highly stable molecule) from the ylide (136) during the reaction.

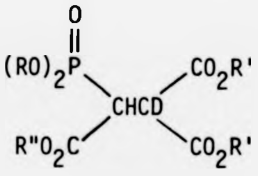
The reaction of the ylides (142) with hydrogen chloride to give the phosphonates (138) can now be readily understood, and a proposed mechanism is shown in Fig. 38 with the sites of labelling as indicated.



(142) (138)

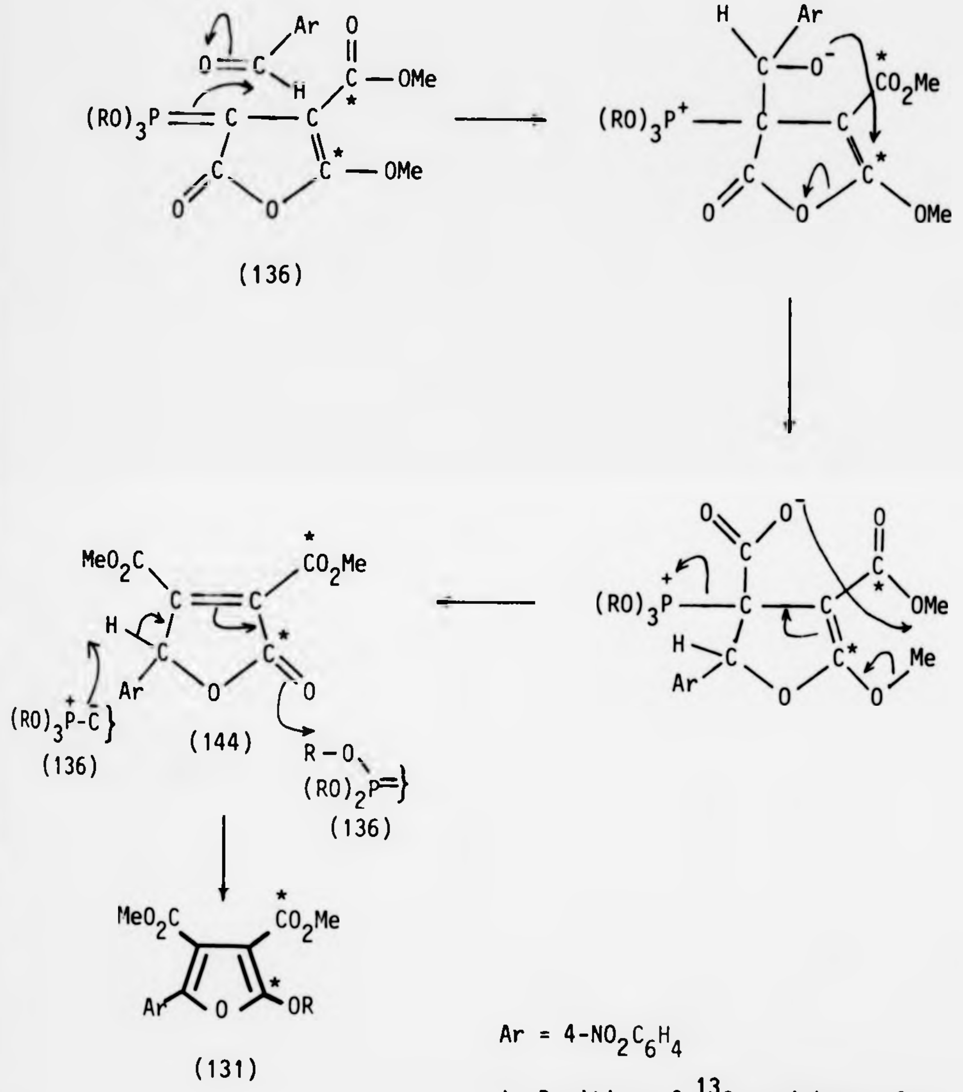
Fig. 38

The mechanism of the formation of the phosphonates (138) (Figs. 37 and 38) is consistent with the observation that the treatment of the ylide (136) with deuteriated alcohol followed by hydrogen chloride, led to the formation of the phosphonate (143) in which the α-carbon was protonated and the β-carbon deuteriated.



(143)

Although this effect was not readily observable in the ^{13}C n.m.r. spectrum of the deuteriated phosphonates (143), due to overlap of the β-carbon resonance signals with the methoxy carbon resonances, this problem was overcome by the use of the corresponding ethyl system



Ar = 4-$NO_2C_6H_4$

* Position of ^{13}C enrichment from the preparation of the ylide (136) using ^{13}C enriched carbon dioxide [see earlier Discussion].

Fig. 39

Finally, the formation of the phosphonate giving a signal at δ_P 21.3 p.p.m. is explained since it arises as a result of the protonation and dealkylation of a molecule of ylide (136) by the initially formed furanone (144) (Fig. 39).

The ease of formation of the furans (131) via the ylides (136) has already been commented upon and a number of analogues of (131) were prepared by this method in good yield [see earlier Discussion]. In view of this it was decided to investigate further the scope of this reaction as a means of producing other substituted furans. For this reason the reaction of the ylide (136; R = Me) with a variety of carbonyl compounds, including acetophenone, trifluoroacetophenone, 4-nitroacetophenone, methyl formate, formaldehyde, and benzaldehyde was investigated. However, these failed to give significant quantities of the desired furans. Instead a competing reaction occurred which was subsequently shown to be due to the thermal rearrangement of the ylide (136; R = Me). Efforts to increase the rate of reaction of the ylide (136; R = Me) with a given carbonyl compound by, for example, increasing the reaction temperature were therefore unsuccessful since they also increased the rate of rearrangement of the ylide (136; R = Me).

5. INVESTIGATION OF THE PRODUCTS FROM THE THERMAL REARRANGEMENT OF THE YLIDE (136; R = Me).

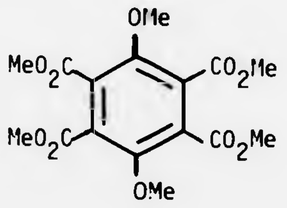
In order to investigate the thermal rearrangement of the ylide (136; R = Me) a sample of the ylide in toluene was heated under reflux overnight. This treatment was found to lead to the formation of a number of phosphorus-containing components, although the phosphonate at δ_P 13.58 p.p.m. was the major signal, corresponding to approximately half of the total ^{31}P n.m.r. signal. Some trimethyl phosphite was also formed together with some dimethyl methylphosphonate, presumably due to the thermal rearrangement of the trimethyl phosphite.

Attempts were then made to separate the various components formed during the thermal rearrangement of the ylide (136; R = Me) by chromatography. Preliminary work with preparative layer chromatography on silica using an ethyl acetate/petroleum ether mixture as eluant enabled two components to be isolated; a white solid which contained no phosphorus, and an oil giving a ^{31}P n.m.r. chemical shift of δ_P 13.58 p.p.m. which was shown to be the same material as that originally observed in the crude reaction mixture. This separation procedure was repeated on a larger scale using medium pressure column chromatography to obtain sufficient quantities of these two components to enable them to be studied in greater detail.

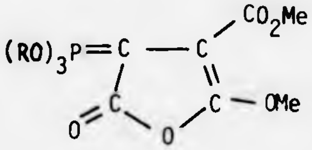
5.1 Investigation of the non-phosphorus-containing component.

The white solid which was isolated gave only two singlets in the ^{1}H n.m.r. spectrum at 3.85 and 3.90 p.p.m. which were both consistent with the presence of methoxy groups. The lower field signal, that at 3.90 p.p.m., had an integral twice that of the signal at 3.85 p.p.m. The ^{13}C n.m.r. spectrum of the solid was also obtained under conditions where minimum distortion of the signal intensities would be expected to occur. This showed only five carbon resonances. Two, those at δ_C 52.94 and 64.29 p.p.m., clearly arose from sp^3 hybridised carbons and their quartet character in the proton-coupled ^{13}C n.m.r. spectrum confirmed that they were indeed methoxy carbons. As expected one of these signals, that at δ_C 52.94 p.p.m., was twice the intensity of the other. The lowest field signal, that at δ_C 164.45 p.p.m., which was of comparable intensity to the higher field methoxy signal, showed a long range coupling to a methyl group (J_{CH} 4 Hz) and was assigned to the carbonyl carbons in at least two methyl ester groups.

Long range proton coupling to a methyl group (J_{CH} 4 Hz) was also observed on the resonance at δ_C 151.46 p.p.m. This signal was of similar intensity to that of the methoxy signal at δ_C 64.29 p.p.m. and was therefore assigned to the carbon adjacent to this methoxy group. The remaining signal, that at δ_C 130.17 p.p.m. showed no long range coupling to protons and was of similar intensity to the signals at δ_C 164.45 and 52.94 p.p.m. The ultra-violet spectrum of the unknown solid indicated that the system was highly conjugated [λ_{max} n.m. (ϵ mol^{-1} dm^2) 208 (272000); 306 (38000)], possibly suggesting an aromatic system. The infra-red spectrum confirmed the presence of ester carbonyl at 1748 cm^{-1} and also the ether linkage (1165 cm^{-1}). This information, together with the observed molecular ion at m/e 370 in the mass spectrum enabled the white solid to be identified as tetramethyl 3,6-dimethoxybenzene-1,2,4,5-tetracarboxylate (145) although the mechanism for the formation of this material is not readily apparent. Approximately 3.5% of this material had been formed during the thermal decomposition of the ylide (136; R = Me).



(145)

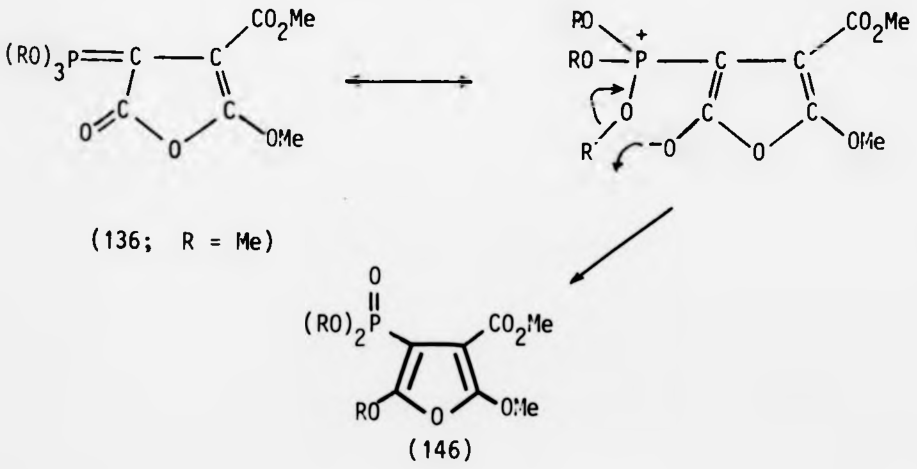


(136)

5.2 Identification of the organophosphorus compound arising from the thermal rearrangement.

The material produced on thermal rearrangement of the ylide (136; R = Me) was quickly identified as a dimethyl phosphonate, due to its chemical shift of δ_P 13.58 p.p.m. and the multiplicity of this resonance signal in the proton-coupled ^{31}P n.m.r. spectrum. This was supported by the ^1H n.m.r. spectrum [see Experimental] which not only showed the presence of three singlets corresponding to three different methoxy groups, but also a methoxy doublet due to the two methoxy groups still attached to the phosphorus.

The ^{13}C n.m.r. spectrum (Table 37), on the other hand, was more complex but entirely consistent with that for the furan (146; R = Me) which we would expect to result from the thermal rearrangement of the ylide (136; R = Me) (see Fig. 40). This rearrangement product also gave a combustion analysis consistent with the formation of the furan (146; R = Me). (See Plate 22).



(136; R = Me)

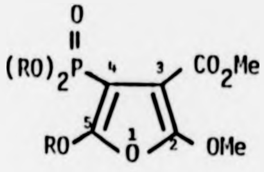
(146)

Fig. 40

TABLE 37

^{13}C N.m.r. spectral data.

Dimethyl 2,5-dimethoxy-3-methoxycarbonyl-4-furanylphosphonate (146; R = Me)



(146)

δ^a

	R = Me	^{13}C {^{31}P}^{c}
P-OR	52.81(6)	q^d
Me	51.48	q
Me	59.74	q
C-5 R	60.28^b	q
C-4	85.20(223)	s^{d,e}
C-3	93.30(10)	s^d
C-5	155.06(17)	q^d
C-2	155.54(15)	q^d
C=O	161.82	q

[a] Shifts in p.p.m. from Me_4Si; J_{PC} in Hz in parentheses; [^{2}H]Chloroform, 26 °C.

[b] Signal broadened, exhibits a small J_{PC} coupling.

[c] Multiplicity from the ^{13}C n.m.r. spectrum with {^{31}P} selective irradiation at δ(^{31}P) 13.58 p.p.m.

[d] Phosphorus coupling removed.

[e] Signal broadened, exhibits residual coupling.

^{13}C N.m.r. spectrum of dimethyl 2,5-dimethoxy-3-methoxycarbonyl-4-furanylphosphonate (146; R = Me) (proton decoupled).

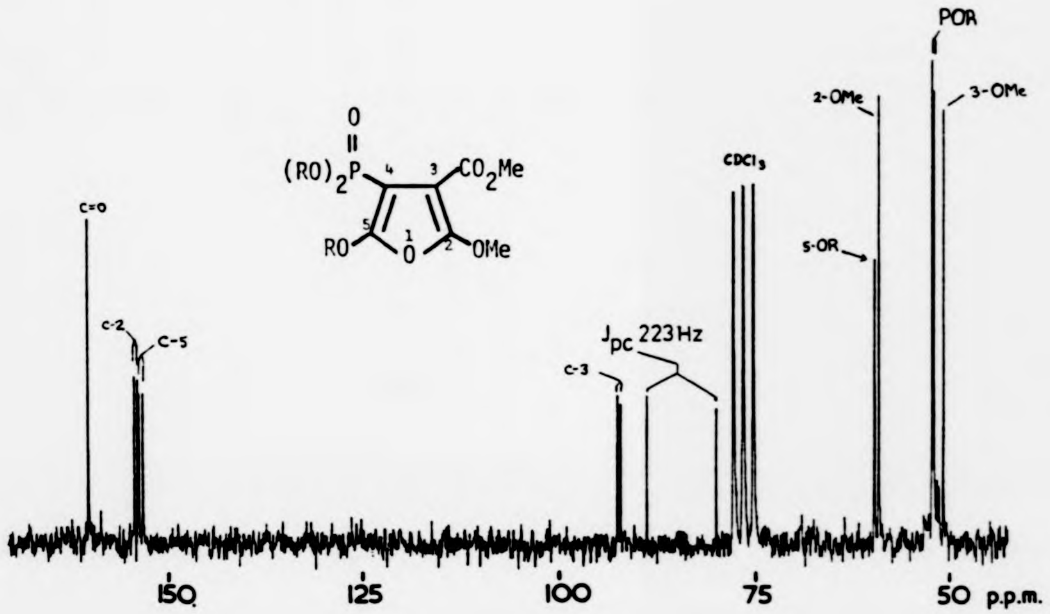
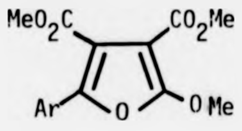


Plate 22

Attempts were therefore made to prepare the furan (146) by an independent synthesis, so that its structure could be confirmed. However, these attempts proved to be less successful than those which had resulted in the formation of the furan (131; R = Me).



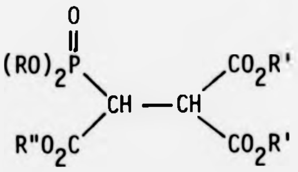
(131)

Ar = 4-$NO_2C_6H_4$

5.3 Attempted preparation of the furan (146; R = Me) by an independent route.

5.3.1 By cyclisation of a phosphonate.

In view of the availability of the phosphonate (138; R,R'R" = Me) initial attempts to prepare the furanylphosphonate (146; R = Me) involved the cyclisation of this phosphonate. The dehydration of the phosphonate (138; R,R',R" = Me) was attempted by using both phosphorus pentoxide and phosphorus pentachloride, but without success. No sign of the desired cyclisation was observed by ^{31}P n.m.r. spectroscopy.



(138)

5.3.2 Via the acetylenic phosphonate, ethyl (diethoxyphosphinyl)-propynoate.

The next method investigated involved the use of the acetylenic phosphonate (147), prepared from ethyl propiolate by the method of Hall and Trippett[76] (see Fig. 41). It was hoped that the reaction of this material with 2,5-dimethoxyfuran, followed by a retro Diels-Alder reaction would give the desired furanylphosphonate (148) (see Fig. 41), an analogue of the furan (146; R = Me) prepared by thermal rearrangement of the ylide (136; R = Me).

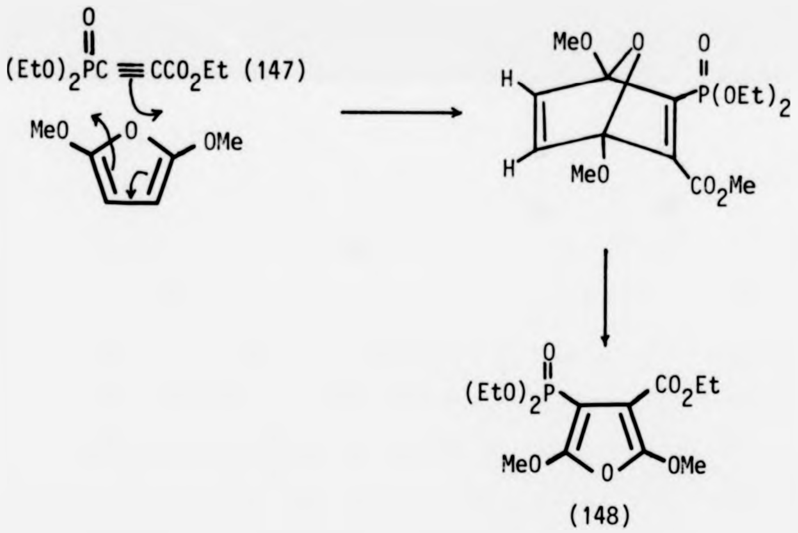


Fig. 41

Unfortunately, the preparation of the 2,5-dimethoxyfuran proved to be difficult and once formed this material was found to be rather unstable.

Initial attempts to prepare 2,5-dimethoxyfuran by the dehydration of dimethyl succinate were unsuccessful, and therefore a route based on 2,5-dibromofuran was investigated. We approached the preparation of 2,5-dibromofuran by the reaction of bromine with the sodium salt of 5-bromo-2-furancarboxylate but this invariably resulted in the reisolation of the furoic acid and the formation of the desired furan in only low yield. It was concluded that the pH of the aqueous reaction mixture was becoming progressively more acidic as the reaction proceeded and that this was resulting in the precipitation of the furoic acid before bromination could occur. In an attempt to avoid this, sodium carbonate was added to the reaction mixture, but this had only a detrimental effect on the reaction. The 2,5-dibromofuran was eventually prepared in about 55% yield by having excess sodium hydroxide present in the aqueous reaction mixture.

The nucleophilic substitution of the bromine atoms in 2,5-dibromofuran by methoxy groups was then investigated under a variety of conditions. Elevated temperatures tended to result in polymerisation, but by allowing the dibromofuran to react with sodium methoxide at room temperature it was possible to prepare a reaction mixture which contained some 2,5-dimethoxyfuran. Unfortunately, this material rapidly polymerised so that the proposed Diels-Alder reaction with the acetylenic phosphonate (147) could not be carried out.

Attempts to make the 2,5-dibromofuran undergo a Diels-Alder reaction with dimethyl acetylenedicarboxylate were also investigated to see if it might be feasible to approach the preparation of the furanylphosphonate (148) via 2,5-dibromofuran, but these were unsuccessful. The heating of the reaction mixtured led to the formation of a tetramer of dimethyl acetylenedicarboxylate, this being indicated by the mass spectrum of the product which gave a molecular ion at m/e 568.

It may be possible to prepare the furanylphosphonate (148) via an analogous route to that used for the preparation of the furan (131; R = Me), (see Fig. 42), however, this route has not been investigated.

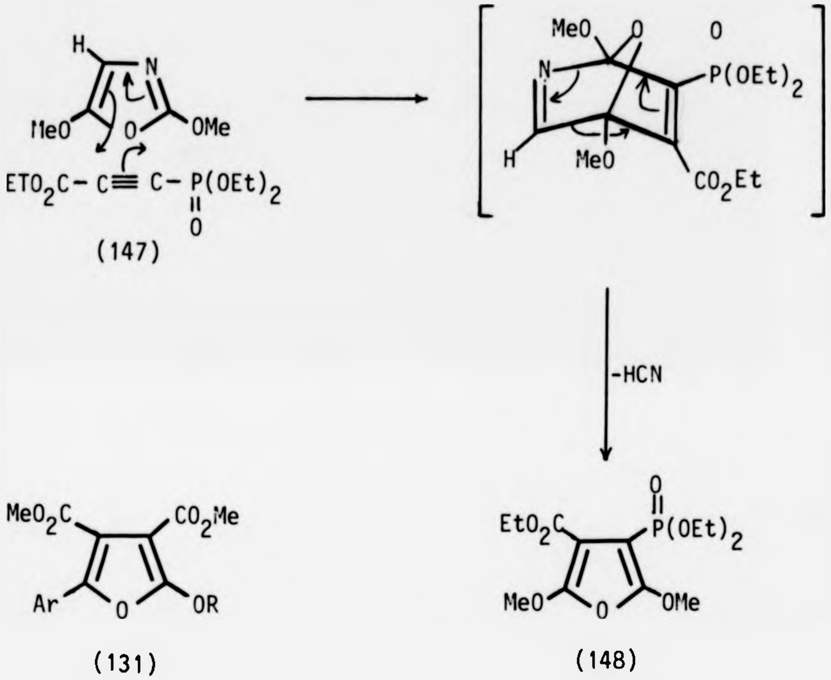
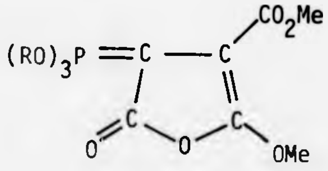


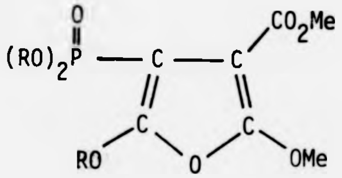
Fig. 42

5.4 Attempts to reduce the ease of thermal rearrangement of the ylide.

Work[64] has shown that in general the trimethoxy phosphoranes are much more susceptible to thermal rearrangement than those with larger alkoxy substitutents such as the triethoxy phosphoranes. For this reason the ylide (136; R = Et) was prepared in the hope that the thermal rearrangement of the ylide might be suppressed to some extent enabling some increase in the reaction of the ylide with carbonyl compounds such as acetophenone and benzaldehyde to take place. However, the ethyl substituted ylide (136; R = Et) was still found to undergo thermal rearrangement to the furylphosphonate (146; R = Et) at (^{31}P) 13.43 p.p.m. in preference to the formation of a furan incorporating the carbonyl compound.



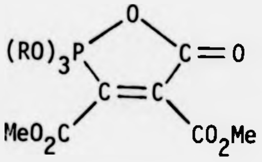
(136)



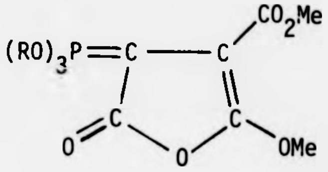
(146)

6. SUMMARY

We have established that the initially proposed structure of the ylide formed on reaction of the "CO_2-adduct" (108) with trialkyl phosphites was incorrect and that it has the isomeric structure (136).

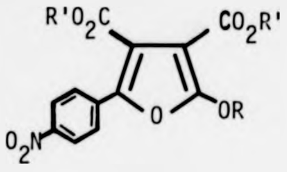


(108)

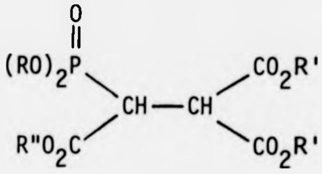


(136)

We have also shown that the ylide (136) can be readily converted either into certain interesting furans such as (131) by reaction with 4-nitrobenzaldehyde, or into phosphonates of the general type (138) by its reaction with alcohol. We have found that both these types of compound to be difficult to synthesise in good yield by other method.

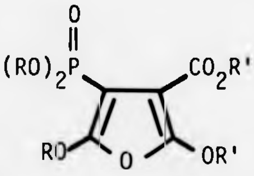


(131)



(138)

We have investigated the possibility of reacting other carbonyl compounds with the ylide (136), but without success. In these latter cases the ylide (136) thermally rearranged to the furanylphosphonate (146) before the desired reaction with the carbonyl group could occur. Attempts to stabilise the ylide to reduce its tendancy to rearrange to a furan have so far been unsuccessful, but there is still scope for further work in this area.



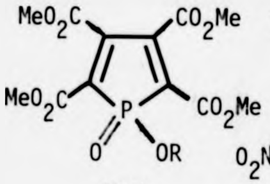
(146)

CHAPTER 4

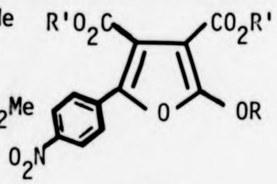
Preliminary Studies of the Reaction of Trialkyl Phosphites with Electrophilic Acetylenes other than Dimethyl Acetylenedicarboxylate.

1. INTRODUCTION

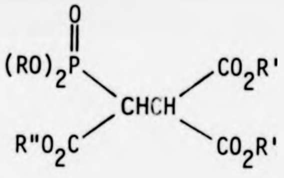
We have already demonstrated that a number of interesting compounds can be prepared by routes which initially involve the reaction of a trialkyl phosphite with dimethyl acetylenedicarboxylate. Thus, for example, compounds such as the oxo-phospholes (91), the furans (131) and the phosphonates (138) have all been prepared in this way.



(91)



(131)



(138)

In view of this it was clearly desirable to try to assess whether such reaction routes would be followed by other electrophilic acetylenes. If this were the case, this would increase the synthetic utility of these routes by enabling substituents other than an ester group to be incorporated into the final products. With this aim in mind we have prepared limited quantities of several electrophilic acetylenes to assess their behaviour with trialkyl phosphites. However, from our work with dimethyl acetylenedicarboxylate it was appreciated that such studies might require substantial work before conditions were established which led to the formation of pure compounds, due to the wide range of potential products which could arise in such reaction. The following preliminary studies were therefore carried out with the aim of trying to establish whether there would be scope for further work in this area.

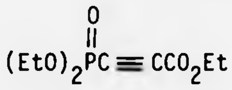
2. DICYANOACETYLENE (149).

$$NCC{\equiv}CCN$$

(149)

Dicyanoacetylene was prepared by the method of Blomquist[82] and, due to its instability, was used as soon as possible after preparation. Unfortunately, however, the reaction of this acetylene with trimethyl phosphite was not easy to control and gave a mixture of products. Preliminary studies therefore suggest that it will not be easy to obtain clean products in this reaction. However, it would be unwise to draw any final conclusions until further studies at low temperature have been carried out.

3. ETHYL (DIETHOXYPHOSPHINYL)PROPYNOATE (147).

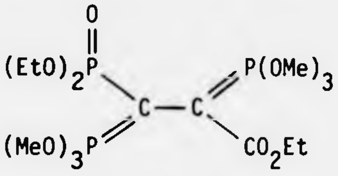


$$(EtO)_2\overset{\overset{O}{\|}}{P}C{\equiv}CCO_2Et$$

(147)

The preparation of ethyl (diethoxyphosphinyl)propynoate (147) was carried out by the method of Trippett.[76] The initial studies of the reaction of trimethyl phosphite with two molar equivalents of ethyl (diethoxyphosphinyl)propynoate (147) were carried out at low temperatures (about -70 °C) in an attempt to minimise the number of products formed. However, no reaction was observed at these temperatures. Furthermore, even when the reaction mixture was allowed to warm to room temperature the reaction was rather slow.

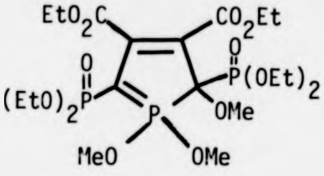
The product formed under these conditions gave a complex ^{31}P n.m.r. spectrum consistent with that of the tri-phosphorus compound (150) which contains both the 1,2-diphosphorane unit and a phosphonate group.

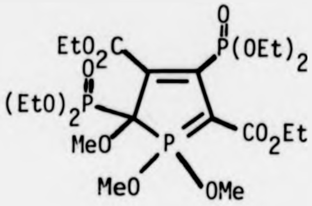


(150)

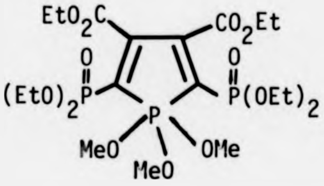
Two isomeric structures for the 1,2-diphosphorane (150) are clearly visible in the ^{31}P n.m.r. spectrum, and these arise as a result of restricted rotation about the bond to the ethoxycarbonyl group.[5,6] The ^{31}P n.m.r. spectrum is thus that of two overlapping three-spin systems. In one system there is a coupling between the ylide group at δ_P 60.1 and the phosphonate group at δ_P 32.5 of J_{PP} 171 Hz. The second ylide group at δ_P 63.64 has no observed coupling to the phosphonate group but a coupling to the ylide group at δ_P 60.1 of J_{PP} 8.5 Hz. The other isomer has a phosphonate grouping at δ_P 31.34 with a coupling to the ylide group at δ_P 58.82 of about J_{PP} 174 Hz. The coupling between the two ylide groups at δ_P 60.87 and δ_P 58.8 was the same as that observed in the other isomer (J_{PP} 8.5 Hz).

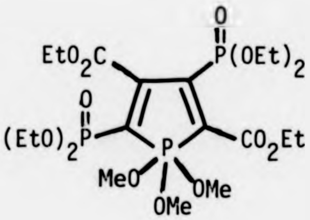
The formation of (150) would indicate that the 1:1 intermediate initially formed in this reaction prefers to react with trimethyl phosphite rather than a second molecule of ethyl (diethoxyphosphinyl)-propynoate (147). To encourage the formation of species derived from one molecule of phosphite and two of the acetylene (147), it was found to be necessary to add the phosphite to excess acetylene in toluene at 80 °C. Under these conditions the ^{31}P n.m.r. spectrum of the reaction mixture showed two doublets of doublets at δ_P 98.1 and δ_P 96.5 p.p.m. which we believe to be derived from the cyclic ylides (151) and (152). The doublet of doublet character in these signals is in agreement with that expected to arise due to the presence of the two additional phosphorus atoms in these molecules.


(151)


(152)

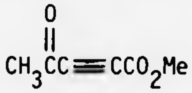
The phosphorus atoms derived from the acetylene (147) gave rise to a number of signals in the phosphonate region of the ^{31}P n.m.r. spectrum (15-22 p.p.m.). On the basis of the couplings observed, the signal at δ_P 98.1 (d of d, J_{PP} 59, 38 Hz) is tentatively assigned to structure (151), while that at δ_P 96.5 (d of d, J_{PP} 31, 16 Hz) is more consistent with a structure such as (152). Since these cyclic ylides would be derived from the corresponding η^5-phospholes (153) and (154), it is possible that the small triplet at δ_P -22.4 (t, J_{PP} 30 Hz) and the small doublet at δ_P -33.5 (d, J_{PP} 45 Hz) may be due to these five-coordinate phosphoranes.


(153)


(154)

Interestingly, if the n^5-phospholes (153) and (154) have withstood heating to 80 °C they are clearly more stable than those derived from dimethyl acetylenedicarboxylate. In conclusion, although the use of an asymmetrical acetylene increases the number of potential products which can arise from the reaction with a trialkyl phosphite, the preliminary work on ethyl (diethoxyphosphinyl)propynoate (147) would suggest that there is clearly scope for further work with this acetylene. Efforts to trap the proposed 1:1 intermediate in this reaction by the use of carbon dioxide to give a CO_2-adduct have so far been unsuccessful.

4. METHYL 4-OXO-PENT-2-YNOATE (155).

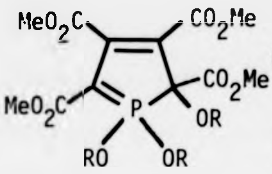


$$CH_3\overset{O}{\overset{\|}{C}}C{\equiv}CCO_2Me$$

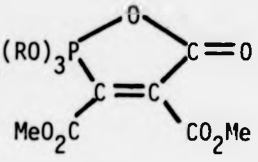
(155)

Methyl 4-oxo-pent-2-ynoate (155) was prepared by the oxidation of methyl 4-hydroxypent-2-ynoate which was synthesised by the reaction of the Grignard of the tetrahydropyranyl ether of but-1-yn-3-ol with methyl chloroformate. Preliminary studies suggest that the reaction of this acetylene (155) with trimethyl phosphite follows a similar reaction pathway to that observed with dimethyl acetylenedicarboxylate since the reaction leads to the formation of a component giving a broad singlet at $\delta(^{31}P)$ 86 p.p.m., similar to that observed for the cyclic ylides (91). However, additional reaction involving the participation of the carbonyl group on the alkyne may also be occurring since ^{31}P n.m.r. spectroscopy showed the presence of a component giving two doublets at δ_P 20.4 and

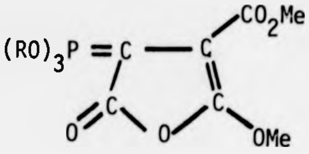
-29.1 p.p.m., which was not observed in our studies with dimethyl acetylenedicarboxylate. Further work is required to identify this product.



(91)



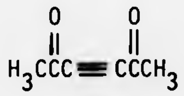
(108)



(136)

In the presence of carbon dioxide the reaction was diverted from its normal path to give a component which had a ^{31}P n.m.r. chemical shift of -52 p.p.m. This is consistent with the formation of a "CO_2-adduct" analogous to (108). Moreover, as with the adduct (108) previously studied, the addition of further trimethyl phosphite to this "CO_2-adduct" caused the ^{31}P n.m.r. signal at -52 p.p.m. to be replaced by one at approximately 70 p.p.m. together with one corresponding to trimethyl phosphate. This would suggest that an ylide analogous to (136) is being formed. If this ylide were to react in the same way to that of the ylide (136) this would provide a route to some interesting products.

5. HEX-3-YNE-2,5-DIONE (156).

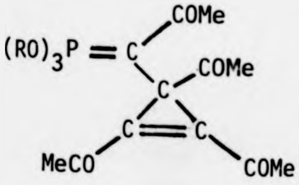


$$H_3C\overset{O}{\overset{\|}{C}}C\equiv C\overset{O}{\overset{\|}{C}}CH_3$$

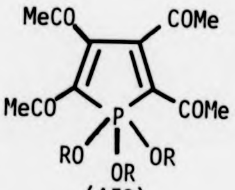
(156)

The diketone, hex-3-yne-2,5-dione (156), was prepared by the oxidation of hex-3-yne-2,5-diol which, before it became commercially available, was obtained by us by the action of acetaldehyde on the di-Grignard reagent prepared from acetylene. The oxidation of the diol to the diketone (156) could not be satisfactorily achieved in a single step and had to be carried out via the 5-hydroxy-hex-3-yn-2-one. However, considerable difficulties were experienced with the preparation and isolation of the diketone (156). The oxidation of a mixture of hex-3-yne-2,5-diol and 5-hydroxyhex-3-yn-2-one with chromic acid was found to be the least unsatisfactory procedure to produce (156), although even then the reaction was unpredictable giving varying yields of product. Considerable polymerisation of the diketone (156) also appeared to occur during distillation, further reducing the yield of this acetylene. The diketone (156) was used as soon as possible after its preparation.

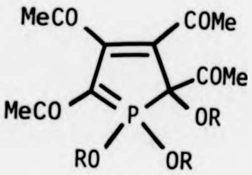
Once again the reaction of hex-3-yne-2,5-dione (156) with trimethyl phosphite appeared to proceed by an analogous pathway to that observed with dimethyl acetylenedicarboxylate. Thus, the addition of trimethyl phosphite to hex-3-yne-2,5-dione (156) in toluene at -70 °C led to the formation of a signal at $\delta(^{31}P)$ 57.65 (decet, J_{PH} 10 Hz) which is assigned to the ylide (157). Warming the sample to +10 °C caused the signal δ_P 57.65 to be replaced by one at δ_P -43.32, consistent with the expected rearrangement of the ylide to the phosphorane (158).



(157)



(158)



(159)

The phosphorane at $\delta(^{31}P)$ -43.32 (158) appeared reluctant to undergo rearrangement to the cyclic ylide (159). Heating the phosphorane (158) led to decomposition but there was no evidence for the formation of substantial quantities of the cyclic ylide (159). However, since we have previously shown that phosphoranes such as (158) can be used as precursors for oxo-phospholes, it should be possible to use the phosphorane (158) in a similar way.

General Conclusion.

In conclusion, it would appear that there are grounds to suppose that the work described in this thesis can be extended to electrophilic acetylenes other than dimethyl acetylenedicarboxylate and that there is still much scope for further studies in this area.

EXPERIMENTAL

THE REACTION OF DIMETHYL ACETYLENEDICARBOXYLATE WITH AN EXCESS OF SOME TERTIARY PHOSPHORUS COMPOUNDS.

Preparation of 1,2-diphosphoranes.

1,2-Bismethoxycarbonylethane-1,2-bis(trimethoxyphosphorane) (88; R = Me).

A solution of dimethyl acetylenedicarboxylate (4.6 g, 0.032 mol) in dry diethyl ether (50 cm^3) was added slowly over a period of 2.5 h to a stirred solution of trimethyl phosphite (8 g, 0.064 mol), in dry ether (50 cm^3), cooled in an ice-water bath, under nitrogen. A fine yellow precipitate settled from the solution. This was filtered off, washed with dry ether, and then dried under vacuum (0.01 mm Hg). The product (12.23 g; 97%) was shown to be the desired 1,2-diphosphorane (88; R = Me), m.p. 87-90 °C. [Found: C, 37.2; H, 6.13; $M^{+\cdot}$ 390. $C_{12}H_{24}O_{10}P_2$ requires C, 36.92; H, 6.21%; M,390]. $\delta(^{31}P)$ 64.2, 62.6 (d, J_{PP} 10 Hz), 61.3 (d, J_{PP} 10 Hz), 60.15 [see Plate 1].

Reactions of 1,2-bismethoxycarbonylethane-1,2-bis(trimethoxyphosphorane). (88; R = Me).

1.1 Reaction with water.

The 1,2-diphosphorane (88; R = Me) (3 g, 7.7 mmol) was dissolved in water (20 cm^3) and left to stand at room temperature. Over a period of several days ^{31}P n.m.r. spectroscopy showed the formation of 3 components at δ_P 23.62, 21.88, and 2.40 p.p.m. in the ratio of 29:42:29 respectively and the disappearance of those signals corresponding to the starting material. The aqueous solution was extracted with chloroform (25 cm^3) and the extract then dried over anhydrous magnesium sulphate. After filtering the chloroform was removed on a rotary evaporator to give an oil. On standing crystals formed in the oil. These were filtered off and then washed repeatedly with dry diethyl ether before being dried (room temperature, 0.01 mm Hg). The resulting colourless crystals (0.8 g, 29%) were identified as a mixture of two diastereoisomers of tetramethyl 1,2-bismethoxycarbonylethane-1,2-diphosphonate (17; R = Me) [Found: C, 33.20; H, 5.71. $C_{10}H_{20}O_{10}P_2$ requires C, 33.15; H, 5.57%]. $\delta(^{31}P)$ 21.8 (24%), 21.55 (76%). $\delta(^{13}C)$ 44.1 (m, α-C), 53.0 (OMe), 53.7 (d, J_{PC} 4 Hz, POMe), 53.8 (d, J_{PC} 3 Hz, POMe), 167.1 (C = O).

1.2 Reaction with hydrogen bromide (anhydrous).

A solution of the diphosphorane (88; R = Me) (2 g, 5.1 mmol) in a mixture of dry diethyl ether (15 cm^3) and chloroform (5 cm^3) was treated with anhydrous hydrogen bromide until the yellow colour of the solution had been discharged. Removal of the solvent on a rotary evaporator gave a viscous oil which solidified on standing. The waxy solid was broken up under dry diethyl ether and the resulting white solid then filtered off. After washing with some diethyl ether the solid was dried under reduced pressure (0.01 mm Hg) at room temperature. Tetramethyl 1,2-bismethoxycarbonylethane-1,2-diphosphonate (17; R = Me) was obtained as a white hygroscopic solid (1.75 g, 94%). [Found: C, 32.9; H, 5.6; M^+, 362. $C_{10}H_{20}O_{10}P_2$ requires C, 33.15; H, 5.6%, M, 362]. $\delta(^{31}P)$ 21.8, 21.55 (diastereoisomers) ratio 2:8 respectively. ^{13}C N.m.r. spectroscopy showed the compound to be identical to the 1,2-diphosphonate prepared by treatment of the diphosphorane with water.

1.3 Reaction with concentrated hydrochloric acid.

To the 1,2-diphosphorane (88; R = Me) (5.95 g, 0.015 mol) was slowly added cold concentrated hydrochloric acid (40 cm^3).

evaporator to give an oil. On standing crystals formed in the oil. These were filtered off and then washed repeatedly with dry diethyl ether before being dried (room temperature, 0.01 mm Hg). The resulting colourless crystals (0.8 g, 29%) were identified as a mixture of two diastereoisomers of tetramethyl 1,2-bismethoxycarbonylethane-1,2-diphosphonate (17; R = Me) [Found: C, 33.20; H, 5.71. $C_{10}H_{20}O_{10}P_2$ requires C, 33.15; H, 5.57%]. $\delta(^{31}P)$ 21.8 (24%), 21.55 (76%). $\delta(^{13}C)$ 44.1 (m, α-C), 53.0 (OMe), 53.7 (d, J_{PC} 4 Hz, POMe), 53.8 (d, J_{PC} 3 Hz, POMe), 167.1 (C = O).

1.2 Reaction with hydrogen bromide (anhydrous).

A solution of the diphosphorane (88; R = Me) (2 g, 5.1 mmol) in a mixture of dry diethyl ether (15 cm^3) and chloroform (5 cm^3) was treated with anhydrous hydrogen bromide until the yellow colour of the solution had been discharged. Removal of the solvent on a rotary evaporator gave a viscous oil which solidified on standing. The waxy solid was broken up under dry diethyl ether and the resulting white solid then filtered off. After washing with some diethyl ether the solid was dried under reduced pressure (0.01 mm Hg) at room temperature. Tetramethyl 1,2-bismethoxycarbonylethane-1,2-diphosphonate (17; R = Me) was obtained as a white hygroscopic solid (1.75 g, 94%). [Found: C, 32.9; H, 5.6; M^+, 362. $C_{10}H_{20}O_{10}P_2$ requires C, 33.15; H, 5.6%, M, 362]. $\delta(^{31}P)$ 21.8, 21.55 (diastereoisomers) ratio 2:8 respectively. ^{13}C N.m.r. spectroscopy showed the compound to be identical to the 1,2-diphosphonate prepared by treatment of the diphosphorane with water.

1.3 Reaction with concentrated hydrochloric acid.

To the 1,2-diphosphorane (88; R = Me) (5.95 g, 0.015 mol) was slowly added cold concentrated hydrochloric acid (40 cm^3).

The mixture was allowed to stand at room temperature for 2 days and the hydrochloric acid was then removed on a rotary evaporator (40 °C at 16 mm Hg). The resulting oil was dissolved in a little water and the solution treated with decolourising charcoal. The charcoal was filtered off and the water removed under reduced pressure. Final traces of water were removed under higher vacuum (0.01 mm Hg) to give a viscous oil which solidified on standing. The solid was broken up under dry diethyl ether and then filtered off and dried. 1,2-Bishydroxycarbonylethane-1,2-diphosphonic acid (89) was obtained as a white hygroscopic solid (2.54 g, 60%). [Found: C, 17.1; H, 3.35. $C_4H_8O_{10}P_2$ requires C, 17.3; H, 2.9%]. $\delta(^{31}P)$ (DMSO-d_6) 21.4, J_{PH} 12 Hz; $\delta(^{31}P)$ (D_2O) 15.8; $\delta(^{31}P)$ (D_2O) 13.1, Na salt. $\delta(^{13}C)$ (DMSO-d_6) 46.3 (d, J_{PC} 115 Hz), 169.5; $\delta(^{13}C)$ (D_2O) 48.0 (d, J_{PC} 110 Hz), 126.

1.4 Attempted reaction with 4-nitrobenzaldehyde.

A solution of the 1,2-diphosphorane (88; R = Me) (2 g) in dry toluene was heated under reflux with 4-nitrobenzaldehyde (1.55 g) for 5 h in a nitrogen atmosphere. ^{31}P N.m.r. spectroscopy showed no change in the spectrum of the 1,2-diphosphorane, and ^{1}H n.m.r. spectroscopy showed that the 4-nitrobenzaldehyde had also been unaffected.

1.5 Attempted reaction with iodoethane.

A solution of the 1,2-diphosphorane (88; R = Me) (3 g) in iodoethane (20 cm^3) was heated under reflux for 6 h in a nitrogen atmosphere. ^{31}P N.m.r. spectroscopy showed no change in the spectrum of the 1,2-diphosphorane.

1.6 The effect of heating the 1,2-diphosphorane (88; R = Me).

1.6.i A sample of the crude 1,2-diphosphorane (88; R = Me) (12 g) was dissolved in toluene (30 cm^3) and heated under reflux for 5.5 h in a nitrogen atmosphere. No thermal rearrangement of the 1,2-diphosphorane was observed.

1.6.ii A sample of the 1,2-diphosphorane (88; R = Me) (12 g) was heated at 150 °C under nitrogen for 7 h. ^{31}P N.m.r. spectroscopy showed no change in the ^{31}P n.m.r. spectrum of the 1,2-diphosphorane (88; R = Me) and no sign of the claimed rearrangement product tetramethyl 2,3-bismethoxycarbonylbutane-2,3-diphosphonate (14).

1,2-Bismethoxycarbonylethane-1,2-bis(triethoxyphosphorane) (88; R = Et).

A solution of dimethyl acetylenedicarboxylate (6 g, 0.04 mol) in dry diethyl ether (25 cm^3) was added dropwise over 2.5 h to a stirred solution of triethyl phosphite (2.57 g, 0.02 mol) in dry diethyl ether (25 cm^3) cooled in an ice-water bath. The solvent was removed on a rotary evaporator (50 °C at 16 mm Hg) and the resulting oil was then heated under vacuum (50 °C at 0.1 mm Hg) until volatile components had been removed. ^{31}P N.m.r. spectroscopy showed the resulting oil to be the desired 1,2-diphosphorane (7.57 g, 89%), δ_P 59.1, 58.0 (d, J_{PP} 10 Hz), 56.3 (d, J_{PP} 10 Hz), 55.38, in a good state of purity. The oil was triturated with a variety of solvents, in an attempt to crystallise the product, but without success. Attempts to distil the oil under vacuum led to decomposition. [Found: C, 44.6; H, 7.6. $C_{18}H_{36}O_{10}P_2$ requires C, 45.6; H, 7.7%].

Reactions of 1,2-bismethoxycarbonylethane-1,2-bis(triethoxyphosphorane). (88; R = Et).

2.1 Reaction with hydrogen bromide (anhydrous).

Treatment of the 1,2-diphosphorane (88; R = Et) (8.24 g, 17 mmol) in dry diethyl ether (50 cm^3) with anhydrous hydrogen bromide led to protonation and dealkylation to give tetraethyl 1,2-bismethoxycarbonylethane-1,2-diphosphonate (17; R = Et) as an oil (6.79 g, 95%). This was shown to be a mixture of two diastereoisomers $\delta(^{31}P)$ 19.4 and 19.1, in the ratio of 1:7 respectively.

2.2 Reaction with concentrated hydrochloric acid.

Treatment of the 1,2-diphosphorane (88; R = Et) (1.48 g, 3 mmol) with concentrated hydrochloric acid (10 cm^3) initially led to the formation of tetraethyl 1,2-bismethoxycarbonylethane-1,2-diphosphonate (17; R = Et). Heating of the resultant solution under reflux for 5 h led to further hydrolysis and formation of 1,2-bishydroxycarbonylethane-1,2-diphosphonic acid (89). The product was identical to the 1,2-diphosphonic acid prepared from 1,2-bismethoxycarbonylethane-1,2-bis(trimethoxyphosphorane) (88; R = Me) and was purified by the same procedure. (Yield 0.47 g, 57%). [Found: C, 17.5; H, 3.2. $C_4H_8O_{10}P_2$ requires C, 17.3; H, 2.9%].

Attempts to prepare tetramethyl 2,3-bismethoxycarbonylbutane-2,3,diphosphonate (14) by the method of Griffin and Mitchell.[12]

The reaction of Griffin and Mitchell[12] was repeated and monitored by ^{31}P n.m.r. spectroscopy. Thus, dimethyl acetylenedicarboxylate (7.1 g, 0.05 mol) was added dropwise to a stirred solution of trimethyl phosphite (12.4 g, 0.1 mol) in dry diethyl ether (100 cm^3) under nitrogen. During the addition the temperature of the reaction was maintained below 10 °C by cooling with an ice-water bath. The resulting mixture was then stirred for 1 h at room temperature. ^{31}P N.m.r. spectroscopy showed the presence of the 1,2-diphosphorane (88; R = Me) as a group of signals δ_P 60 - 65 in about 80% yield. The reaction mixture was then heated under reflux for 1 h (^{31}P n.m.r. spectroscopy indicated that this produced no change in the composition of the mixture), and then the solvent was removed (15 mm Hg, 50 °C bath). Attempted distillation of the remaining oil at 190 °C and 0.5 mm Hg resulted in decomposition of the sample and the formation of a large number of products. There was no n.m.r. evidence for the formation of significant quantities of the diphosphonate (14).

The formation of 1,2-diphosphoranes by the reaction of dimethyl acetylenedicarboxylate with excess dialkyl phosphonites

1,2-Bismethoxycarbonylethane-1,2-bis(dimethoxyphenylphosphorane) (90; R = OMe, R' = Ph).

A solution of dimethyl acetylenedicarboxylate (0.14 g, 1 x 10^{-3} mol) in chloroform (1 cm^3) was added slowly dropwise to a solution of dimethyl phenylphosphonite (0.35 g, 2 x 10^{-3} mol) in chloroform (2.5 cm^3). ^{31}P N.m.r. spectroscopy showed the resulting solution to contain the desired 1,2-diphosphorane (90; R = OMe, R' = Ph) in good yield. For ^{31}P n.mr. spectral data see Table 1.

1,2-Bismethoxycarbonylethane-1,2-bis(dimethoxymethylphosphorane) (90; R = OMe, R' = Me).

The 1,2-diphosphorane (90; R = OMe, R' = Me) was prepared using dimethyl methylphosphonite (2 x 10^{-3} mol) by the method previously described for the preparation of the 1,2-diphosphorane (90; R = OMe, R' = Ph). For ^{31}P n.m.r. spectral data see Table 1.

1,2-Bismethoxycarbonylethane-1,2-bis(diethoxyphenylphosphorane) (90; R = OEt, R' = Ph).

The 1,2-diphosphorane (90; R = OEt, R' Ph) was prepared under similar conditions to those used to prepare the 1,2-diphosphorane (90; R = OMe, R' = Ph) using diethyl phenylphosphonite (2×10^{-3} mol). The 1,2-diphosphorane (90; R = OEt, R' = Ph) was prepared in good yield, for ^{31}P n.m.r. spectral data see Table 1.

1,2-Bismethoxycarbonylethane-1,2-bis(methyldiphenylphosphorane) (90; R = Ph, R' = Me).

The 1,2-diphosphorane (90; R = Ph, R' = Me) was prepared using methyl diphenylphosphinite by the method previously described for the preparation of the 1,2-diphosphorane (90; R = OMe, R' = Ph). For ^{31}P n.m.r. spectral data see Table 1.

FORMATION OF A 1,4-DIPHOSPHORANE FROM THE REACTION OF TRIMETHYL PHOSPHITE WITH DIMETHYL ACETYLENEDICARBOXYLATE.

Tetramethyl 1,4-Bis(trimethoxyphosphoranylidene)-2-butene-1,2,3,4-tetracarboxylate (68; R = OMe)

To an agitated solution of dimethyl acetylenedicarboxylate (0.22 g, 1.5×10^{-3} mol) in [$^{2}H_{8}$]toluene (1 cm^3) in a sealed vessel (25 cm^3 volume), fitted with a rubber septum, was slowly added, using a syringe, a solution of trimethyl phosphite (0.38 g, 3.1×10^{-3} mol) in [$^{2}H_{8}$]toluene (1.5 cm^3). ^{31}P N.m.r. spectroscopy showed the presence of three components, tetramethyl

1,1,2-trimethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Me), trimethyl phosphate, and a component giving a ^{31}P n.m.r. signal at 52.6 p.p.m. On standing for a few days a pale yellow precipitate formed, this was filtered off, washed first with toluene, then with diethyl ether and finally recrystallised from toluene. The solid was identified by n.m.r. spectroscopy as the phosphorane (68; R = OMe) (0.17 g, 41.2%), m.p. 86 - 87 °C. [Found: C, 40.8; H, 5.7. $C_{18}H_{30}O_{14}P_2$ requires C, 40.6; H, 5.7%]. $\delta(^{31}P)$ ([^{2}H]chloroform) 51.7, ([$^2H_8$]toluene) 52.6. $\delta(^1H)$ 3.54 (s), 3.64 (s), 3.84 (d, J_{PH} 12 Hz); {^{31}P}Sel. 51.7 p.p.m. 3.88 (s). $\delta(^{13}C)$ 55.39 (d, J_{PH} 4 Hz, POMe), 55.26 (d), J_{PH} 4 Hz, POMe), 51.82 (Me), 49.82 (Me), 171.77 (br, C = O), 84-102 (ill-resolved signal, C = C), 58.73 (ill-resolved signal, P = C). I.R. (chloroform) cm^{-1}: 1745, 1645.

THE REACTION OF SOME TERTIARY PHOSPHORUS COMPOUNDS WITH AN EXCESS OF DIMETHYL ACETYLENEDICARBOXYLATE.

Trialkoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonyl-cyclopropenyl)methylene]phosphoranes (92).

Trimethoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonyl-cyclopropenyl)methylene]phosphorane (92; R = Me).

A solution of trimethyl phosphite (0.12 g, 1 mmol) in dry [$^2H_8$]toluene (0.5 cm^3) was cooled to about -70 °C and then added to a solution of dimethyl acetylenedicarboxylate (0.25 g, 2 mmol) in dry [$^2H_8$]toluene (2 cm^3) also at about -70 °C in an n.m.r. tube (10 mm diam). The tube was then quickly transferred into the n.m.r. probe previously cooled to -50 °C and the reaction monitored at this temperature. ^{31}P N.m.r. spectroscopy showed that the trialkyl phosphite reacted over a period of about 2 h to give an essentially quantitative yield of the ylide (92; R = Me). The structure of the ylide (92; R = Me) was established by low temperature (-50 °C) ^{31}P n.m.r. and ^{13}C n.m.r. spectroscopy (see Tables 2 and 3).

Triethoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonyl cyclopropenyl)methylene]phosphorane (92; R = Et).

The ylide (92; R = Et) was prepared under similar conditions to those used to prepare the ylide (92; R = Me), using triethyl phosphite (0.16 g, 1 mmol). The ^{31}P n.m.r. spectrum of the ylide (92; R = Et) is given in Table 2.

Triisopropoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonyl cyclopropenyl)methylene]phosphorane (92; R = Pr^{i}).

The ylide (92; R = Pr^{i}) was prepared by the method previously described for the ylide (92; R = Me) using triisopropyl phosphite (0.2 g, 1 mmol). The ^{31}P n.m.r. spectrum of (92; R = Pr^{i}) is given in Table 2.

Tetramethyl 1,1,1-Trialkoxy-n^{5}-phosphole-2,3,4,5--tetracarboxylates (95).

Tetramethyl 1,1,1-Trimethoxy-n^{5}-phosphole-2,3,4,5--tetracarboxylate (95; R = Me).

A solution of the ylide, trimethoxy[methoxycarbonyl--(1,2,3-trismethoxycarbonylcyclopropenyl)methylene]phosphorane (92; R = Me), in [^{2}H$_{8}$]toluene at -50 °C was allowed to warm up to -10 °C. At this temperature rapid rearrangement occurred to give the n^{5}-phosphole (95; R = Me). The ^{13}C and ^{31}P n.m.r. spectra of the n^{5}-phosphole (95; R = Me) are given in Table 4. The n^{5}-phosphole

(95; R = Me) was unstable at room temperature with a half-life of about 10 to 12 min in toluene.

Tetramethyl 1,1,1-Triethoxy-n^5-phosphole-2,3,4,5-tetracarboxylate (95; R = Et).

The n^5-phosphole (95; R = Et) was prepared from the ylide (92; R = Et) under similar conditions to those used for the n^5-phosphole (95; R = Me). The ^{13}C and ^{31}P n.m.r. spectra of the n^5-phosphole (95; R = Et) are given in Table 4.

Tetramethyl 1,1,1-Triisopropoxy-n^5-phosphole-2,3,4,5,-tetracarboxylate (95; R = Pr^i).

The n^5-phosphole (95; R = Pr^i) was prepared from the ylide (92; R = Pr^i) under similar conditions to those used to prepare the n^5-phosphole (95; R = Me). The ^{31}P n.m.r. spectrum of the n^5-phosphole (95; R = Pr^i) showed δ_P([$^2H_8$]toluene, -50 °C) -48.5 (q, J_{PH} 10 Hz).

Tetramethyl 1,1,2-Trialkoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylates (91).

Tetramethyl 1,1,2-Trimethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Me).

A solution of trimethyl phosphite (2 g, 16 x 10^{-3} mol) in dry diethyl ether (15 cm^3) at about -50 °C was added to a solution of dimethyl acetylenedicarboxylate (4.58 g, 0.03 mol) in diethyl ether (15 cm^3) also at -50 °C. The mixture was allowed to warm to room temperature and then kept at this temperature for several hours. The ether was decanted off to leave a viscous oil. This oil was gently warmed under reduced pressure (0.5 mm Hg) to remove any volatile components present leaving the cyclic ylide (91; R = Me) (4.51 g, 68.5%). [Found: C, 43.8; H, 5.4. $C_{15}H_{21}O_{11}P$ requires

C, 44.1; H, 5.2%]. The ^{13}C and ^{31}P n.m.r. spectra of the cyclic ylide (88; R = Me) are given in Tables 6 and 7 respectively.

Tetramethyl 1,1,2-Triisopropoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Pr^i).

A solution of triisopropyl phosphite (0.18 g, 9 x 10^{-4} mol) in dry toluene (5 cm^3) at -70 °C was rapidly added to a solution of dimethyl acetylenedicarboxylate (0.25 g, 1.7 x 10^{-3} mol) in dry toluene (5 cm^3) also at -70 °C. The two solutions were thoroughly mixed and then allowed to stand at -70 °C for 30 min before being allowed to warm up to room temperature. The solvent was removed under diminished pressure and the residual oil then heated at 50 °C at 0.1 mm Hg to remove any volatile components present. The resulting viscous oil gradually crystallised and was then washed with ether to give the desired cyclic ylide (91; R = Pr^i) (0.34 g, 79%), m.p. 109-111 °C. [Found: C, 51.4; H, 6.9. $C_{21}H_{33}O_{11}P$ requires C, 51.2; H, 6.8%]. δ(^{1}H) 1.1-1.6 (complex, CMe), 3.6 (OMe), 3.6 (OMe), 3.88 (OMe), 4.09-5.09 (complex, CH). The ^{13}C and ^{31}P n.m.r. spectra of the cyclic ylide (91; R = Pr^i) are given in Tables 6 and 7 respectively. Yields of the ylide greater than 90% were obtained in later experiments.

Tetramethyl 1,1,2-Triethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Et).

The cyclic ylide (91; R = Et) was prepared by the method previously described for (91; R = Pr^i) and isolated as a white solid (4.95 g, 62%), m.p. 92-94 °C. [Found: C, 47.85; H, 6.2. $C_{18}H_{27}O_{11}P$ requires C, 48.0; H, 6.05%]. δ(^{1}H) 1.2 (t, J_{HH} 7 Hz), 1.33 (t, J_{HH} 7 Hz), 1.42 (br), 3.61 (OMe), 3.65 (OMe), 3.75 (OMe), 3.92 (OMe), 4.33 (q, J_{HH} 7 Hz). For ^{13}C and ^{31}P n.m.r. spectral data see Tables 6 and 7.

Rearrangement of trimethoxy[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)methylene]phosphorane (92; R = Me) in the presence of glacial acetic acid.

1,2,3,4-Tetramethoxycarbonyl-1-(dimethoxyphosphinyl)-1,3-butadiene (97).

A solution of trimethyl phosphite (1.3 g, 0.01 mol) in dry toluene (40 cm^3) at -50 °C was added to a solution of dimethyl acetylenedicarboxylate (3.0 g, 0.02 mol) in toluene (40 cm^3) also at -50 °C. The mixture was vigorously shaken and left to stand for 2 h at -50 °C. A solution of glacial acetic acid (1.5 cm^3) in toluene (10 cm^3) at -50 °C was then added, the mixture again shaken and allowed to stand for a further ½ h at -50 °C whereupon it was allowed to warm gradually to room temperature. The solvent was removed under reduced pressure (16 mm Hg, 50 °C) leaving a dark viscous oil (4.4 g). ^{31}P N.m.r. spectroscopy showed one major component at δ_P 10.59. Preparative layer chromatography on silica gel using ethyl acetate as eluant gave the desired product which crystallised on standing (1.61 g, 41%), m.p. 87-89 °C. [Found: C, 42.7; H, 4.9%; M^+, 394. $C_{14}H_{19}O_{11}P$ requires C, 42.6; H, 4.9%; M, 394]. $\delta(^{31}P)$ 10.6 (septet, J_{PH} 12 Hz); $\delta(^1H)$ 3.58-3.88 (18H, s), 6.95 (1H, s). For ^{13}C n.m.r. spectral data see Table 5.

Dialkoxyphenyl[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)methylene]phosphorane (102).

Diethoxyphenyl[methoxycarbonyl-(1,2,3-trismethoxycarbonylcyclopropenyl)methylene]phosphorane (102; R = Et, R' = Ph).

A solution of diethyl phenylphosphonite (0.2 g, 1 mmol) in dry [$^2H_8$]toluene (0.5 cm^3) was cooled to about -70 °C and then added to a solution of dimethyl acetylenedicarboxylate (0.28 g, 2 mmol) in dry [$^{2}H_{8}$]toluene (2 cm^{3}) also at -70 °C in an n.m.r. tube (10 mm diam.). The contents of the tube were shaken, then rapdily cooled in liquid nitrogen and the frozen sample placed in the n.m.r. probe cooled to -70 °C. ^{31}P N.m.r. spectroscopy showed that after a period of 30 min at -70 °C the ylide (102; R = Et, R' = Ph) (see Table 8) had been formed in essentially quantitative yield. The structure of this ylide was confirmed by ^{13}C n.m.r. spectroscopy (see Table 9) by comparison with the ^{13}C n.m.r. spectrum of the ylide (92; R = Me) prepared from trimethyl phosphite.

Dimethoxyphenyl[methoxycarbonyl-(1,2,3-trismethoxycarbonyl-cyclopropenyl)methylene]phosphorane (102; R = Me, R' = Ph).

The ylide (102; R = Me, R' = Ph) was prepared from dimethyl phenylphosphonite under similar conditions to those used to prepare the ylide (102; R = Et, R' = Ph). An almost quantitative yield of the ylide (102; R = Me, R' = Ph) was achieved at -70° at a rate four times slower than that achieved for the analogous ylide (102; R = Et, R' = Ph). The ^{31}P n.m.r. spectrum of the ylide (102; R = Me, R' = Ph) is given in Table 8.

Tetramethyl 1,1-Diethoxy-1-phenyl-η^{5}-phosphole-2,3,4,5--tetracarboxylate (98).

The ylide (102; R = Et, R' = Ph) was prepared as previously described and monitored by ^{31}P n.mr. at -70 °C in the n.m.r. probe. After 1½ h at -70 °C, 30% of the ylide (102; R = Et, R' = Ph) had undergone rearrangement to the η^{5}-phosphole (98; R = Et, R' = Ph). The structure of the η^{5}-phosphole was then established by low temperature (-70 °C) ^{13}C n.m.r. spectroscopy (see Table 10). The ^{31}P n.m.r. spectral data of the η^{5}-phosphole (98; R = Et, R' = Ph) is given in Table 10. For (98; R = Me, R' = Ph) $\delta(^{31}P)$ -34.9.

Tetramethyl 1,2-Dialkoxy-1-phenyl-2H-1λ^5-phosphole-2,3,4,5--tetracarboxylates (100).

Tetramethyl 1,2-Diethoxy-1-phenyl-2H-1λ^5-phosphole-2,3,4,5--tetracarboxylate (100; R = Et, R' = Ph).

A solution of diethyl phenylphosphonite (0.8 g, 4 x 10^{-3} mol) in dry toluene (8 cm^3) at -50 °C was quickly added to a solution of dimethyl acetylenedicarboxylate (1.15 g, 8 x 10^{-3} mol) in dry toluene (8 cm^3) also at -50 °C. The mixture was shaken and then allowed to stand at -50 °C for 30 min before being allowed to warm up to room temperature. ^{31}P N.m.r. spectroscopy indicated the presence of only the desired product (100; R = Et, R' = Ph) (δ_P 83.7) in the reaction mixture. The solvent was removed under reduced pressure and the resulting material warmed at 50 °C under high vacuum (0.1 mm Hg) to remove any volatile impurities. The resulting oil was taken up in a little dry ether and the desired product was then precipitated by careful addition of hexane. The product was filtered off and dried by warming at 56 °C under vacuum (0.1 mm Hg). The desired product (100; R = Et, R' = Ph) was obtained as a yellow-orange solid (1.8 g, 92%), m.p. 57-60 °C. [Found: C, 54.5; H, 5.75. $C_{22}H_{27}O_{10}P$ requires C, 54.8; H, 5.65%]. The ^{13}C n.m.r. spectrum is given in Table 12.

Tetramethyl 1,2-Dimethoxy-1-phenyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R = Me, R' = Ph).

The cyclic ylide (100; R = Me, R' = Ph) was prepared from dimethyl phenylphosphonite under similar conditions to those used to prepare the cyclic ylide (100; R = Et, R' = Ph) (90%). The ^{31}P and ^{13}C n.m.r. spectra are given in Tables 11 and 12 respectively.

Preparation of dimethyl methylphosphonite and its reaction with an excess of dimethyl acetylenedicarboxylate.

1.1 Prepared by the method of Hoffman and Moore.[77]

A mixture of superdry methanol (6.29 g, 0.18 mol) and pyridine (14.2 g, 0.18 mol) was added dropwise with stirring to a solution of methylphosphonous dichloride (10 g, 0.08 mol) in diethyl ether (30 cm^3) under nitrogen whilst maintaining the temperature of the solution below 20 °C by cooling in an ice-bath. The reaction mixture was then stirred for 2 h at room temperature. The base hydrochloride was then filtered off under reduced pressure and washed with cold diethyl ether (20 cm^3). The ether was removed under reduced pressure with no external heating and the residual liquid then distilled (50 °C bath, 276 mm Hg) (lit.,[78] b.p. 62-65 °C, 300 mm Hg) to give the phosphonite (0.76 g, 9%). $\delta(^{31}P)$ 183.3 (dec, J_{PH} 10 Hz). $\delta(^{1}H)$ 1.19 (d, J_{PH} 8 Hz), 3.52 (d, J_{PH} 11 Hz).

1.2 Prepared by the method of Maeir.[78]

N,N,N,N-Tetramethyl methylphosphonous diamide

A solution of methylphosphonous dichloride (14.3 g, 0.12 mol) in diethyl ether (30 cm^3) was added dropwise to a solution of dimethylamine (35 g, 0.77 mol) in diethyl ether (150 cm^3), under nitrogen and cooled in an ice-bath. The precipitated base hydrochloride was filtered off and the ether evaporated under nitrogen gas. Distillation of the resulting liquid gave the diamide (64 °C, 47 mm Hg) (lit.,[78] b.p. 62 °C, 45 mm Hg) (14.2 g, 88%). $\delta(^{31}P)$ 87.1. $\delta(^{1}H)$ 1.28 (d, J_{PH} 7 Hz, PMe), 2.70 (d, J_{PH} 9 Hz, NMe).

Dimethyl methylphosphonite.

To N,N,N,N-tetramethyl methylphosphonous diamide (14.2 g, 0.1 mol) was added dry distilled methanol (7 g) and the reaction followed by

^{31}P n.m.r. spectroscopy. After 20 min all the diamide had reacted to form N,N-dimethyl (methoxy)methylphosphonous amide at δ_P 141.8 and after a further, 1 h the formation of the phosphonite was complete. Distillation (42 °C, 300 mm Hg) (lit.,[78] 62-65 °C, 300 mm Hg) gave the phosphonite (4.62 g, 40%), $\delta(^{31}P)$ 183.3.

2. Tetramethyl 1,2-Dimethoxy-1-methyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R,R' = Me).

A solution of dimethyl methylphosphonite (0.5 g, 4.6 x 10^{-3} mol) in dry toluene (5 cm^3) at -70 °C was quickly added to a solution of dimethyl acetylenedicarboxylate (1.31 g, 9.2 x 10^{-3} mol) in dry toluene (5 cm^3) also at -70 °C. The mixture was shaken and then allowed to stand at -70 °C for 20 min before being allowed to warm to room temperature. ^{31}P N.m.r. spectroscopy showed the product to contain approximately 80% of the desired cyclic ylide (δ_P 97.5). Addition of hexane to the reaction mixture caused the precipitation of a white solid which was filtered off. The solid was redissolved in the minimum of chloroform and reprecipitated with hexane. Finally, the solid was suspended in hexane and the mixture heated to near boiling and then allowed to cool. The precipitated cyclic ylide (100; R,R' = Me) was filtered off and dried to give a white solid (1.27 g, 70%), m.p. 131-134 °C. [Found: C, 45.55; H, 5.7. $C_{15}H_{21}O_{10}P$ requires C, 45.9; H, 5.4%]. $\delta(^{31}P)$ 97.4. The ^{13}C n.m.r. spectral data (100; R,R' = Me) is given in Table 13.

Preparation of diallyl acetylenedicarboxylate and its reaction with trimethyl phosphite.

Diallyl acetylenedicarboxylate (109)

A solution of dimethyl acetylenedicarboxylate (10 g, 0.08 mol), p-toluenesulphonic acid (0.6 g) and hydroquinone (0.1 g) in allyl alcohol (40 g; distilled from anhydrous potassium carbonate) was heated on an oil bath at 110 °C in a flask (250 cm^3) fitted with fractionating column and distillation head. The temperature of the oil bath was slowly raised to 130 °C over 2 h so that the allyl alcohol distilled from the reaction flask. The resulting reaction mixture was cooled, then water (50 cm^3) was added and the mixture extracted with diethyl ether (3 x 30 cm^3). The ether extracts were washed with sodium bicarbonate solution and dried ($MgSO_4$). The ether was removed under reduced pressure (15 mm Hg, 40 °C) and the product distilled over hydroquinone (0.1 g) to give the ester (10.7 g, 63%), (b.p. 108-118 °C, 4 mm Hg) (lit.,[71] 112-118 °C, 4 mm Hg). [Found: C, 62.0; H, 5.4. $C_{10}H_{10}O_4$ requires C, 61.8; H, 5.20%]. $\delta(^{13}C)$ 67.19 (OCH_2), 74.54 (α-C), 119.75 (CH_2), 130.21 (CH), 151.10 (C = O).

Reaction of trimethyl phosphite with an excess of diallyl acetylenedicarboxylate (109).

A solution of trimethyl phosphite (0.12 g, 1 x 10^{-3} mol) in $[^2H_8]$toluene (0.5 cm^3) at -70 °C was added to a solution of diallyl acetylenedicarboxylate (0.39 g, 2 x 10^{-3} mol) in $[^2H_8]$toluene (2 cm^3) at -70 °C in an n.m.r. tube (10 mm diameter). The sample was vigorously shaken and then placed in the ^{31}P n.m.r. probe at -70 °C.

Initially, only the ^{31}P n.m.r. signal of trimethyl phosphite (δ_P 140) was observable in the spectrum, however, after 7 min at

-70 °C all the trimethyl phosphite had reacted giving rise to two broad signals. The signal at $\delta(^{31}P)$ 61.4 was identified as the ylide, trimethoxy[prop-2-enoxycarbonyl-(1,2,3-trispropenoxycarbonyl-cyclopropenyl)methylene]phosphorane, while that at $\delta(^{31}P)$ -37.3 was identified as the η^5-phosphole, tetraprop-2-ene 1,1,1-trimethoxy -η^5-phosphole-2,3,4,5-tetracarboxylate. After a further 45 min at -70 °C the ^{31}P n.m.r. signal due to the cyclic ylide (110), tetraprop-2-ene 1,1,2-trimethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate was identified at δ_P 85.04. The solution was then allowed to warm up to -50 °C, and after 100 min at this temperature, when there were no further changes in the ^{31}P n.m.r. spectrum, the solution was allowed to warm to room temperature (26 °C). After 35 min at room temperature conversion to the cyclic ylide $\delta(^{31}P)$ (26 °C) 85.98 was complete. The formation of the cyclic ylide (110) from diallyl acetylenedicarboxylate followed the same course as that for the formation of the cyclic ylides (91) and (100) using dimethyl acetylenedicarboxylate, no abnormal route was observed.

OXO-PHOSPHOLES FROM TRIVALENT PHOSPHORUS COMPOUNDS AND DIMETHYL ACETYLENEDICARBOXYLATE.

1-Oxo-1H-1λ^5-phospholes from η^5-phospholes.

Tetramethyl 1-Methoxy-1-oxo-1H-1λ^5-phosphole-2,3,4,5--tetracarboxylate (111; R = Me).

A solution of trimethyl phosphite (1.31 g, 0.01 mol) in dry diethyl ether (20 cm^3) at -50 °C was rapidly added to a solution of dimethyl acetylenedicarboxylate (3 g, 0.02 mol) in dry diethyl ether (20 cm^3) also at -50 °C. The mixture was kept at this temperature for about 20 min then allowed to warm slowly to -10 °C. Diethyl ether (20 cm^3), saturated with hydrogen bromide (1 g, 0.01 mol), was added to the mixture with shaking. After about 5 min at -10 °C the mixture was allowed to warm to room temperature. The solvent and other volatile components were then removed under reduced pressure (16 mm Hg, 50 °C) to give a viscous oil. A little chloroform was added to make this oil less viscous and the resulting material was then triturated with hexane. This produced a cloudy suspension of the desired product in the hexane above the viscous oil. The hexane was then decanted off and filtered. This procedure was repeated with further quantities of hexane until no further product could be obtained. The oxo-phosphole was obtained as a white solid (1.15 g, 32%). [Found: C, 43.55; H, 4.2. $C_{13}H_{15}O_{15}P$ requires C, 43.1; H, 4.2%]. The ^{13}C n.m.r. and ^{31}P n.m.r. spectra of the oxo-phosphole (111; R = Me) (Table 16) were the same as those of the oxo-phosphole (111; R = Me) prepared by other routes.

Tetramethyl 1-Ethoxy-1-oxo-1H-1λ^5-phosphole-2,3,4,5--tetracarboxylate (111; R = Et).

1.1 A solution of triethyl phosphite (1.7 g, 0.01 mol) in dry diethyl ether (15 cm^3) at below -50 °C was rapidly added to a solution of dimethyl acetylenedicarboxylate (2.91 g, 0.02 mol) also in dry diethyl ether (15 cm^3) at below -50 °C. The mixture was shaken and kept at this temperature for about 30 min and then allowed to warm to -10 °C. Diethyl ether (25 cm^3), saturated with hydrogen bromide (1 g, 0.01 mol) and cooled to -10 °C, was then added to the mixture with shaking. After standing for about 10 min the mixture was allowed to warm to room temperature. The white solid on the sides of the vessel was removed washed with diethyl ether and then dried.

A further crop of the phosphole was obtained by removing the ether from the reaction solution, this left an oil which crystallised on standing. The resulting solid was then washed with diethyl ether and dried. The structure of the oxo-phosphole (111; R = Et) (2.04 g, 54%), m.p. and mixed m.p. 133-135.5 °C, was confirmed by ^{1}H, ^{31}P and ^{13}C n.m.r. spectroscopy (see Table 16).

1.2 A solution of triethyl phosphite (1.7 g, 0.01 mol) in dry diethyl ether (15 cm^3) at -50 °C was quickly added to a solution of dimethyl acetylenedicarboxylate (2.91 g, 0.02 mol) in dry diethyl ether (15 cm^3) at -50 °C. This mixture was then quickly transferred to a thermally insulated pressure-equalised dropping funnel, which was mounted on a 500 cm^3 round-bottomed flask, filled with hydrogen bromide at atmospheric pressure and cooled to about 0 °C. The contents of the pressure-equalised dropping funnel were allowed to drip into the flask whereupon a vigorous reaction was observed. At the end of the addition the contents of the flask were shaken to ensure that the reaction was complete, and then the phosphole which had formed was filtered off and washed with ether. The filtrate and washings were combined and the ether then removed under reduced pressure (16 mm Hg, 50 °C) to give a viscous oil. Trituration of this oil with a little diethyl ether gave a further crop of the oxo-phosphole. The phosphole (111; R = Et) was obtained as a white solid (2.22 g, 59%), m.p. and mixed m.p. 133-135 °C. [Found: C, 44.45; H, 4.6. $C_{14}H_{17}O_{10}P$ requires C, 44.7; H, 4.5%]. $\delta(^{1}H)$ 1.40 (t, J_{PH} 7 Hz), 3.88 (s), 4.39 (d of q, J_{PH} 10 Hz, J_{HH} 7 Hz). For ^{13}C and ^{31}P n.m.r. spectra see Table 16.

Tetramethyl 1-Oxo-1-phenyl-1H-1λ^5-phosphole-2,3,4,5--tetracarboxylate (112; R' = Ph).

A solution of diethyl phenylphosphonite (1 g, 5 mmol) in dry toluene (10 cm^3) at -70 °C was quickly added to a solution of dimethyl acetylenedicarboxylate (1.43 g, 0.01 mol) in dry toluene (10 cm^3) also at -70 °C. The mixture was shaken then allowed to stand for about 1 h at -70 °C. Hydrogen bromide gas was then bubbled into the toluene solution at -70 °C until the orange-brown colour of the solution had been discharged. The resulting solution was allowed to warm to room temperature. ^{31}P N.m.r. spectroscopy indicated that the reaction mixture contained the desired oxo-phosphole (112; R' = Ph) as the major component (approx. 40% of the total ^{31}P n.m.r. signal). Most of the toluene was removed under reduced pressure (50 °C, 16 mm Hg) and dry diethyl ether added. White hygroscopic crystals separated, these were filtered off, washed with dry diethyl ether and then dried under vacuum to give the oxo-phosphole (112; R' = Ph) (0.23 g, 11%). [Found: C, 52.7; H, 4.65. $C_{18}H_{17}O_9P$ requires C, 52.95; H, 4.2%]. The structure of the oxo-phosphole (112; R' = Ph) was confirmed by ^{13}C and ^{31}P n.m.r. spectroscopy (see Table 17).

Attempts to isolate further quantities of the oxo-phosphole (112; R' = Ph) led to the isolation of the oxo-2-phospholene (113; R' = Ph) (0.44 g, 21%). See later experimental section.

Tetramethyl 1-Methyl-1-oxo-1H-1λ^5-phosphole-2,3,4,5--tetracarboxylate (112; R' = Me).

A solution of dimethyl methylphosphonite (0.1 g, 1 mmol) in dry toluene (0.5 cm^3) was cooled to -70 °C and then added to a solution of dimethyl acetylenedicarboxylate (0.25 g, 2 mmol) in dry toluene (2 cm^3) also at -70 °C in an n.m.r. tube (1 cm diameter). After about 5 h at -70 °C ^{31}P n.m.r. spectroscopy showed the presence of tetramethyl 1,1-dimethoxy-1-methyl-n^5-phosphole-2,3,4,5-tetracarboxylate (98; R,R' = Me) at δ_P -34.3 (about 20% of the total ^{31}P n.m.r. signal intensity). Hydrogen bromide gas was then passed into the sample and ^{31}P n.m.r. spectroscopy confirmed the formation of the oxo-phosphole (112; R' = Me) at δ_P 46.1 (about 15% of the total ^{31}P n.m.r. signal intensity).

1-Oxo-1H-1λ^5-phospholes from 2H-1λ^5-phospholes.

Tetramethyl 1-Isopropoxy-1-oxo-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (111; R = Pr^i.

A solution of tetramethyl 1,1,2-triisopropoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Pr^i) (1.7 g, 3.4 x 10^{-3} mol) in toluene (30 cm^3) was cooled in an ice-bath and then carefully treated with hydrogen bromide gas until the colour of the solution had changed from an orange-red to lime-green. ^{31}P N.m.r. spectroscopy confirmed that none of the cyclic ylide remained in solution. The solvent was removed under reduced pressure and the residue washed with diethyl ether then heated at 50 °C initially at a reduced pressured of 16 mm Hg for approximately 30 min, and then at a lower pressure (0.01 mm Hg) to remove any volatile components. ^{31}P N.m.r. spectroscopy showed the product (1.17 g, 87%) to be the desired oxo-phosphole (111; R = Pr^i), δ_P 34 (d, J_{PH} 9 Hz). δ(^{1}H) 1.36 (d of d, J_{PH} 6 Hz, J_{HH} 5 Hz), 3.82 (s), 3.86 (s), 4.15 - 5.35 (complex). For the ^{13}C n.m.r. spectrum see Table 16. [Found: C, 46.1; H, 5.2. $C_{15}H_{19}O_{10}P$ requires C, 46.15; H, 4.9%].
In later experiments yields were routinely obtained in which the preparation of the oxo-phosphole (111; R = Pr^i) was almost quantitative.

Tetramethyl 1-Ethoxy-1-oxo-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (111; R = Et).

A solution of tetramethyl 1,1,2-triethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Et) (4 g, 9×10^{-3} mol) in toluene (30 cm^3) was treated with hydrogen bromide gas in the manner previously described for (91; R = Pr^i). This resulted in the formation of a number of diastereoisomers of the oxo-phospholene (116; R' = OEt) giving ^{31}P n.m.r. signals in the range δ_P 45.5 - 48.7. The solvent was removed under reduced pressure (16 mm Hg, 50 °C) and the residue heated at 50 °C under lower pressure (0.01 mm Hg) until the decomposition of the oxo-phospholene (116; R' = OEt) was complete. The resulting oil was triturated with ether to give the desired oxo-phosphole (111; R = Et) as a white solid (2.09 g, 63%), m.p. 133 - 135 °C. $\delta(^1H)$ 1.40 (t, J_{HH} 7 Hz), 3.85 (s), 4.36 (d of t, J_{PH} 10 Hz, J_{HH} 7 Hz). For ^{13}C and ^{31}P n.m.r. spectra see Table 16. [Found: C, 44.85; H, 4.5. $C_{14}H_{17}O_{10}P$ requires C, 44.7; H, 4.5%].

Tetramethyl 1-Methoxy-1-oxo-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (111; R = Me).

The oxo-phosphole (111; R = Me) was obtained from tetramethyl 1,1,2-trimethoxy-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (91; R = Me) by the method previously described for (111; R = Et). Slow addition of hexane to a solution of the crude phosphole in chloroform led to the precipitation of the desired oxo-phosphole (111; R = Me) as a white solid (3.6 g, 59%). $\delta(^1H)$ 3.88 (s), 3.99 (d, J_{PH} 12 Hz). For ^{13}C and ^{31}P n.m.r. spectral details see Table 16.

Tetramethyl 1-Oxo-1-phenyl-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (112; R' = Ph).

A solution of the cyclic ylide, tetramethyl 1,2-diethoxy-1-phenyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R = Et, R' = Ph) (1.95 g, 4 mmol) in dry toluene (20 cm^3) and cooled in an ice-bath was carefully treated with anhydrous hydrogen bromide until the ^{31}P n.m.r. spectrum showed the absence of the cyclic ylide and the formation of two protonated intermediates (116; R = Et, R' = Ph) at δ_P ($CDCl_3$) 54.7 and 48.7. The solvent was then removed and the residue heated under reduced pressure (16 mm Hg, 100 °C). After about 1.5 h the formation of the desired oxo-phosphole was complete. The identity of the oxo-phosphole (112; R' = Ph) was confirmed by ^{13}C and ^{31}P n.m.r. spectroscopy (see Table 17) and by comparison with an authentic sample prepared by treatment of the η^5-phosphole (98; R = Et, R' = Ph) with anhydrous hydrogen bromide. The oxo-phosphole (112; R' = Ph) was isolated as the "hydrated system" (113) (1.5 g, 87%, (see later Experimental).

A similar preparation of the oxo-phosphole (112; R' = Ph) was also carried out from tetramethyl 1,2-dimethoxy-1-phenyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R = Me, R' = Ph). Once again, however, it was the "hydrated system" (113) which was eventually isolated.

Preparation of tetramethyl 2-ethoxy-5-hydro-1-oxo-1-phenyl-3-phospholene-2,3,4,5-tetracarboxylate (116; R = Et, R' = Ph).

A sample of the cyclic ylide, tetramethyl 1,2-diethoxy-1-phenyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R = Et, R' = Ph) (1.95 g, 4 mmol) in dry toluene (20 cm^3) was cooled in an ice bath and then carefully treated with anhydrous hydrogen bromide.

When the colour of the solution was discharged from orange to pale-yellow, treatment was stopped. The solvent was then removed under a stream of nitrogen with no external heating. The product was then placed under reduced pressure (0.05 mm Hg), at room temperature to remove volatile components. The desired phospholene (116; R = Et, R' = Ph) was obtained as an oil (1.79 g, 97.6%). [Found: C, 52.8; H, 5.3. $C_{20}H_{23}O_{10}P$ requires C, 52.9; H, 5.1%]. $\delta(^{31}P)$ 54.7 and 48.4. The ^{13}C n.m.r. spectral data for the phospholene (116; R = Et, R' = Ph) is given in Table 21.

Tetramethy 1-Methyl-1-oxo-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (112; R' = Me).

A solution of tetramethyl 1,2-dimethoxy-1-methyl-2H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (100; R,R' = Me) (0.5 g, 1.2×10^{-3} mol) in dry toluene (5 cm^3) was cooled in an ice-bath and then carefully treated with hydrogen bromide gas. The solvent was then removed (16 mm Hg, 55 °C bath) and the resultant oil placed under reduced pressure (0.01 mm Hg, 55 °C) to give the phosphole (0.35 g, 80%). [Found: C, 43.6; H, 4.6. $C_{13}H_{15}O_9P$ requires C, 45.1; H, 4.4%]. $\delta(^{31}P)$ 46.1 (q, $^2J_{PH}$ 15 Hz). For ^{13}C n.m.r. spectral data see Table 22.

5-Hydro-4-hydroxy-1-oxo-phospholes.

Tetramethyl 5-Hydro-4-hydroxy-1-oxo-1-phenyl-2-phospholene-2,3,4,5-tetracarboxylate (113).

A sample of the oxo-phosphole (112; R' = Ph) was left exposed to the atmosphere. After 2 hrs ^{31}P n.mr. indicated that this material had been converted to the oxo-phospholene (113). This product was identified by its ^{13}C and ^{31}P n.m.r. spectra (see Table 18). $\delta(^1H)$

1.64 (br, OH), 3.54 (OMe), 3.69 (OMe), 3.78 (OMe), 3.90 (OMe), 4.18 (d, J_{PH} 27 Hz), 7.48 - 7.92 (m, Ar). [Found: C, 50.7; H, 4.5%; M^+, 426. $C_{18}H_{19}O_{10}P$ requires C, 50.7; H, 4.5%; M, 426]. M.p. 132-133 °C.

Tetramethyl 5-Hydro-4-hydroxy-1-isopropoxy-1-oxo-2-phospholene-2,3,4,5-tetracarboxylate (117).

On exposure to the atmosphere the oxo-phosphole (111; R = Pr^i) was found to absorb moisture to give the oxo-phospholene (117). When the oxo-phosphole (111; R = Pr^i) was in a solid form its conversion to the oxo-phospholene (117) was complete after several hours, however, for solutions of the oxo-phosphole (111; R = Pr^i) in chloroform the conversion often took several days. The oxo-phospholene (117) was identified by its ^{13}C and ^{31}P n.m.r. spectra (see Table 20). [Found: C, 43.9; H, 5.2. $C_{15}H_{21}O_{11}P$ requires C, 44.1; H, 5.2%].

Attempted dehydration of tetramethyl 5-hydro-4-hydroxy-1-oxo-1-phenyl-2-phospholene-2,3,4,5-tetracarboxylate (113; R' = Ph).

1.1 By Dean-Stark dehydration using p-toluenesulphonic acid.

A solution of the oxo-phospholene (113; R' = Ph) (0.1 g, 2.3×10^{-4} mol) in benzene (2.5 cm^3; redistilled, sodium dry) with p-toluenesulphonic acid, monohydrate (0.01 g) was placed under reflux in a flask fitted with a Dean-Stark side-arm. The mixture was monitored by ^{31}P n.m.r. spectroscopy over 6 days. No droplets of water resulted in the side-arm and ^{31}P n.m.r. spectrosocpy indicated that no change had occurred in the spectrum of the oxo-phospholene.

1.2 Using concentrated sulphuric acid

To a solution of the oxo-phospholene (113; R' = Ph) (0.1 g, 2.3×10^{-4} mol) in benzene (3 cm^3; redistilled, sodium dry) was added conc. sulphuric acid (0.5 cm^3) and the mixture refluxed for ½ h. On cooling, fine droplets of an oil separated, the benzene was decanted and the oil taken up in [$^2H_6$] acetone. ^{31}P N.m.r. spectroscopy showed that no change had occurred in the spectrum of the oxo-phospholene (113; R' = Ph).

1.3 Using Calcium hydride.

The reaction was carried out as for the attempted dehydration using conc. sulphuric acid, but with calcium hydride (0.05 g). No dehydration product was observed by ^{31}P n.m.r. spectroscopy.

Attempted reduction of 1-oxo-1-phenyl-1H-1λ^5-phosphole.

Attempted reduction of tetramethyl 1-oxo-1-phenyl-1H-1λ^5--phosphole-2,3,4,5-tetracarboxylate (112; R' = Ph) with trichlorosilane.

To a solution of the oxo-phosphole (112; R' = Ph) (0.2 g, 5 x 10^{-4} mol) in [$^2H_6$] benzene (3 cm^3) in an n.m.r. tube (1 cm diameter) was added triethylamine (distilled CaH_2)^{31}P n.m.r. indicated that this resulted in the formation of numerous components. Fortunately, this decomposition could be avoided by the use of either N-methyl piperidine or pyridine rather than triethylamine as the base. However, even in these latter cases it was found that numerous products were formed when the trichlorosilane (2 drops) in benzene (0.5 cm^3) was added.

Attempted reduction of tetramethyl 1-oxo-1-phenyl-1H-1λ^5--tetracarboxylate (112; R' = Ph) with lithium aluminium hydride.

Tetramethyl 1-oxo-1-phenyl-1H-1λ^5-phosphole-2,3,4,5-tetracarboxylate (112; R' = Ph) (1.27 g, 2.6 x 10^{-3} mol) was dissolved in dry diethyl ether (30 cm^3) and then added slowly to a suspension of lithium aluminium hydride (1.5 g) in diethyl ether (30 cm^3), under nitrogen, with stirring. The resulting mixture was then heated under reflux for 2 h. On cooling ethyl acetate (10 cm^3) was added and the mixture refluxed for a further 15 min. Water (15 cm^3) was then added whilst stirring the mixture, and the organic layer then decanted off, dried ($MgSO_4$) and the solvent removed under reduced pressure (16 mm Hg) with gently warming to give a pungent yellow liquid (0.27 g). ^{31}P N.m.r. spectroscopy showed a large group of signals between δ_P 43.6 - 16.6 and two components at δ_P 1.7 and -122.5 (t, $^1J_{PH}$ 201 Hz). After 30 min the high field signal at δ_P -122.5 was no longer present in the ^{31}P n.m.r. spectrum. The ^{31}P n.m.r. resonance signal at δ_P -122.5 p.p.m. was later identified as being due to phenylphosphine,[75] whilst that at δ_P 1.7 was due to phenylphosphine oxide.

THE REACTION OF TRIVALENT PHOSPHORUS COMPOUNDS WITH DIMETHYL ACETYLENEDICARBOXYLATE IN THE PRESENCE OF CARBON DIOXIDE AND ASSOCIATED REACTIONS.

Reaction of triphenylphosphine with dimethyl acetylenedicarboxylate in the presence of carbon dioxide.

1,2-Dimethoxycarbonyl-1-(triphenylphosphonia)ethene-2-carboxylate (121).

To a stirred solution of dimethyl acetylenedicarboxylate (1.08 g, 7.6 x 10^{-3} mol) in dry diethyl ether (20 cm^3), through which dry carbon dioxide gas was being bubbled, was added dropwise triphenylphosphine (2.0 g, 7.6 x 10^{-3} mol) in dry diethyl ether (20 cm^3). The buff coloured precipitate which formed was filtered off under nitrogen and dried under reduced pressure (0.01 mm Hg, room temperature) to give a quantitative yield of the required 'CO_2-adduct' (121) (3.4 g). $\delta(^{31}P)$ [^2H]chloroform, 0.29.

5-Alkoxy-4-alkoxycarbonyl-2,3-dihydro-3-furanylidenephosphoranes.

2,3-Dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me).

To a solution of dimethyl acetylenedicarboxylate (0.25 g, 1.76 x 10^{-3} mol) in [$^2H_8$]toluene (1.5 cm^3), through which carbon dioxide gas (dried over calcium chloride) was being bubbled, was added dropwise a solution of trimethyl phosphite (0.43 g, 3.5 x 10^{-3} mol) in [$^2H_8$]toluene (1 cm^3). ^{31}P N.m.r. spectroscopy showed an almost quantitative preparation of the phosphorane (136; R,R' = Me) together with an equal quantity of trimethyl phosphate.

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The phosphorane (136; R,R' = Me) was identified by ^{31}P and ^{13}C n.m.r. spectroscopy (see Tables 30 and 31 respectively) and carbon-13 enrichment studies [see later Experimental].

2,3-Dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetriethoxyphosphorane (136; R = Et, R' = Me).

The phosphorane (136; R = Et, R' = Me) was prepared by the method previously described for the phosphorane (136; R,R' = Me) using triethyl phosphite in place of trimethyl phosphite. For ^{31}P and ^{13}C n.m.r. spectral data for the phosphorane see Tables 30 and 31 respectively.

2,3,-Dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetriisopropoxyphosphorane (136; R = Pr^i, R' = Me).

The phosphorane (136; R = Pr^i, R' = Me) was prepared by the method previously described for the phosphorane (136; R,R' = Me), using triisopropyl phosphite in the place of trimethyl phosphite. For ^{31}P and ^{13}C n.m.r. spectral data for the phosphorane (136; R,R' = Me) see Tables 30 and 31 respectively.

2,3-Dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenedimethoxyphenylphosphorane.

The phosphorane, 2,3-dihydro-5-methoxy-4-methoxycarbonyl--3-furanylidenedimethoxyphenylphosphorane was prepared by the method previously described for the phosphorane (136; R,R' = Me) using dimethyl phenylphosphonite, in the place of trimethyl phosphite. ^{31}P N.m.r. spectroscopy showed the quantitative preparation of the dimethoxyphenylphosphorane at δ_P 65.3.

5-Ethoxy-4-ethoxycarbonyl-2,3-dihydro-3-furanylidenetriethoxyphosphorane (136; R,R' = Et).

The phosphorane (136; R,R' = Et) was prepared from triethyl phosphite and diethyl acetylenedicarboxylate following the method previously described for the preparation of the phosphorane (136; R,R' = Me). For ^{31}P and ^{13}C n.m.r. spectral data for the phosphorane (136; R,R' = Et) see Tables 30 and 31 respectively.

1,2,2-Tris(alkoxycarbonyl)ethylidenephosphoranes (142).

1,2,2-Tris(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R',R" = Me).

A solution of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3--furanylidenetrimethoxyphosphorane (136; R,R' = Me) (1.76×10^{-3} mol) in chloroform (2.5 cm^3) was treated with methanol (0.06 g, 1.76×10^{-3} mol). ^{31}P N.m.r. showed that this resulted in the loss of the signal due to the phosphorane (136; R,R' = Me) and the appearance of two new components at lower field. Variable temperature ^{31}P n.m.r. studies demonstrated that these two components were in thermal equilibrium, this being consistent with the behaviour expected for the desired phosphorane (142; R,R',R" = Me) (see Table 35). Cooling of the phosphorane (142; R,R',R" = Me) to -30 °C, resulted in considerable sharpening of the ^{31}P n.mr. signals. On the other hand warming of the phosphorane caused signal broadening and resulted in the eventual coalescence of the two ^{31}P n.mr. signals.

2-Deutero-1,2,2-tris(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R',R" = Me, H2 = [^{2}H]).

This deuteriated sample of the phosphorane (136; R,R',R" = Me, H2 = [^{2}H]) was also prepared, by reacting the phosphorane (136;

R,R',R" = Me) with O-[^{2}H]methanol. For ^{31}P n.m.r. spectral data of the phosphorane (142; R,R',R" = Me, H2 = [^{2}H]) see Table 35.

1-Ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R' = Me, R" = Et).

To a solution of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3--furanylidenetrimethoxyphosphorane (136; R,R' = Me) (1.76 x 10^{-3} mol) in chloroform (2.5 cm^{3}) was added ethanol (0.08 g, 1.8 x 10^{-3} mol). ^{31}P N.m.r. spectroscopy showed the quantitative preparation of the phosphorane (142; R,R' = Me, R" = Et). For ^{31}P and ^{13}C n.m.r. spectral data for the phosphorane (142; R,R' = Me, R" = Et) see Tables 35 and 36 respectively.

2-Deutero-1-ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R' = Me, R" = Et, H2 = [^{2}H]).

This deuteriated sample of the phosphorane (142; R,R' = Me, R" = Et) was prepared in a similar manner to that previously described for the phosphorane (142; R,R' = Me, R" = Et) from the phosphorane (136; R,R' = Me) using O-[^{2}H]ethanol. For ^{31}P n.m.r. spectra data for the phosphorane (142; R,R' = Me, R" = Et, H2 = [^{2}H]) see Table 35.

1,2,2-Tris(ethoxycarbonyl)ethylidenetriethoxyphosphorane (142; R,R',R" = Et).

The phosphorane (142; R,R',R" = Et) was prepared in quantitative yield by treating the phosphorane (136; R,R' = Et) (1.76 x 10^{-3} mol) in chloroform (2.5 cm^{3}) with ethanol (0.08 g, 1.8 x 10^{-3} mol). For ^{31}P and ^{13}C n.m.r. spectral data for the phosphorane (142; R,R',R" = Et) see Tables 35 and 36 respectively.

2-Deutero-1,2,2-tris(ethoxycarbonyl)ethylidenetriethoxyphosphorane (142; R,R',R" = Et, H2 = [^{2}H]).

The deuteriated phosphorane (142; R,R',R" = Et, H2 = [^{2}H]) was prepared by the method previously described for the non-deuteriated phosphorane (142; R,R',R" = Et) using O-[^{2}H]ethanol in place of ethanol. The deuteriated phosphorane (142; R,R',R" = Et, H2 = [^{2}H]) was identified by comparison with the non-deuteriated phosphorane. For ^{13}C n.m.r. spectral data of the phosphorane (142; R,R',R" = Et, H2 = [^{2}H]) see Table 36.

1,2,2-Tris(methoxycarbonyl)ethylidenetriethoxyphosphorane (142; R = Et, R',R" = Me).

The phosphorane (142; R = Et, R',R" = Me) was prepared by reacting the phosphorane (136; R = Et, R' = Me) (1.76×10^{-3} mol) with methanol (1.76×10^{-3} mol). For ^{31}P n.m.r. spectral data for the phosphorane (142; R = Et, R',R" = Me) see Table 35.

1-Ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetriethoxyphosphorane (142; R,R" = Et, R' = Me).

A solution of the phosphorane (136; R = Et, R' = Me) (1.76×10^{-3} mol) in chloroform (2.5 cm^3) was treated with ethanol (0.08 g, 1.8×10^{-3} mol). ^{31}P N.m.r. spectroscopy showed a quantitative preparation of the phosphorane (142; R,R" = Et, R' = Me). For ^{31}P and ^{13}C n.m.r. spectral data of the phosphorane (142; R,R" = Et, R' = Me) see Tables 35 and 36 respectively.

2-Deutero-1-ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetriethoxyphosphorane (142; R,R" = Et, R' = Me, H2 = [^{2}H]).

This deuteriated sample of the phosphorane (142; R,R" = Et, R' = Me) was prepared by the method previously described for the phosphorane (142; R,R" = Et, R' = Me) using O-[^{2}H]ethanol in place of ethanol. For ^{31}P n.m.r. spectral data for the phosphorane (142; R,R" = Et, R' = Me, H2 = [^{2}H]) see Table 35.

Dialkyl 1,2,2-Tris(alkoxycarbonyl)ethylphosphonates.

Dimethyl 1,2,2-Tris(methoxycarbonyl)ethylphosphonate (138; R,R'R" = Me).

A solution of 1,2,2-tris(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R',R" = Me) (0.02 mol) in chloroform (25 cm^{3}) was treated with a few drops of concentrated hydrochloric acid with shaking. The orange colouration of the solution was immediately discharged to a pale yellow. ^{31}P N.m.r. spectroscopy showed the quantitative preparation of a single component. The solvent was then removed under reduced pressure (16 mm Hg, 50 °C bath) to leave a thick oil (6.0 g, 97%), ^{31}P and ^{13}C n.m.r. spectroscopy confirmed that this oil was the desired phosphonate (see Table 32). [Found: C, 38.2; H, 5.2. $C_{10}H_{17}O_{9}P$ requires C, 38.5; H, 5.5%]. The phosphonate (138; R,R',R" = Me) could also be prepared by passing a solution of the phosphorane (142; R,R',R" = Me) in chloroform down a short chromatography column (alumina or silica gel).

Dimethyl 1-Ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylphosphonate (138; R,R' = Me, R" = Et).

The phosphonate (138; R,R' = Me, R" = Et) was prepared from the phosphorane (142; R,R' = Me, R" = Et) by the method previously described for the phosphonate (138; R,R',R" = Me). For ^{31}P and ^{13}C n.m.r. spectral data for the phosphonate (138; R,R' = Me, R" = Et) see Tables 33 and 34 respectively.

Diethyl 1-Ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylphosphonate (138; R,R" = Et, R' = Me).

The phosphonate (138; R,R" = Et, R' = Me) was prepared from the phosphorane (142; R,R" = Et, R' = Me) by the method previously described for the phosphonate (138; R,R',R" = Me). For ^{13}C n.m.r. spectral data of the phosphonate (138; R,R" = Et, R' = Me) see Table 34.

Diethyl 1,2,2-Tris(ethoxycarbonyl)ethylphosphonate (138; R,R',R" = Et).

The phosphonate (138; R,R',R" = Et) was prepared from the phosphorane (142; R,R',R" = Et) by the method previously described for the preparation of the phosphonate (138; R,R',R" = Me). For ^{31}P and ^{13}C n.m.r. spectral data for the phosphonate (138; R,R',R" = Et) see Tables 33 and 34 respectively.

Dimethyl 2-Deutero-1,2,2-tris(methoxycarbonyl)ethylphosphonate (143; R,R',R" = Me).

A solution of 1,2,2-tris(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R',R" = Me) (0.021 mol) (prepared using O-[^{2}H]methanol) in chloroform (25 cm^{3}) was treated with a few drops of concentrated hydrochloric acid with shaking. The solvent was then removed under reduced pressure (16 mm Hg, 50 °C) leaving a thick wax which solidified on standing. Recrystallisation from toluene gave the phosphonate (143; R,R',R" = Me) (5.37 g, 82%), m.p. 76-77 °C. [Found: C, 38.3; H, 5.4. $C_{10}H_{16}DO_{9}P$ requires C, 38.3; H, 5.8%]. $\delta(^{31}P)$ 20.9 (see Table 33). $\delta(^{13}C)$ β-C 49.90 (t, $^{3}J_{CD}$ 21 Hz), (see Table 32).

Diethyl 2-Deutero-1,2,2-tris(ethoxycarbonyl)ethylphosphonate (143; R,R',R" = Et).

The phosphonate (143; R,R',R" = Et) was prepared from the phosphorane (142; R,R',R" = Et) (0.021 mol) generated using O-[^{2}H]ethanol by the method previously described for the phosphonate (143; R,R',R" = Me). $\delta(^{31}P)$ 18.6 (see Table 33). $\delta(^{13}C)$ β-C 50.46 (t, $^3J_{CD}$ 21 Hz), (see Table 34).

Diethyl 2-Deutero-1-ethoxycarbonyl-2,2-bis(methoxycarbonyl)-ethylphosphonate (143; R,R" = Et, R' = Me).

The phosphorane (142; R,R" = Et, R' = Me) (0.021 mol) generated using O-[^{2}H]ethanol [see earlier Experimental] in chloroform (25 cm^3) was treated with a few drops of concentrated hydrochloric acid with shaking. ^{31}P N.m.r. spectroscopy showed the quantitative preparation of the phosphonate (143; R,R" = Et, R' = Me) at δ_P 18.6 (see Table 33). $\delta(^{13}C)$ β-C 50.58 (broadened).

Independent synthesis of dimethyl 1,2,2-tris(methoxycarbonyl)-ethylphosphonate (138; R,R',R" = Me).

Trimethyl phosphonoacetate

A mechanically stirred mixture of trimethyl phosphite (10 g, 0.08 mol) and methyl chloroacetate (8.75 g, 0.08 mol) was heated at 110 °C for 10 h. Unreacted material was removed by distillation (16 mm Hg, 50 °C bath) and the resulting oil fractionally distilled (13.12 g, 90%), b.p. 80-90 °C 0.01 mm Hg. [Found: C, 32.7; H, 5.9. $C_5H_{11}O_5P$ requires C, 33.0; H, 6.1%]. $\delta(^{31}P)$ 21.55 (non, J_{PH} 12 Hz). $\delta(^1H)$ 2.98 (d, J_{PH} 22 Hz), 3.74 (s), 3.80 (d, J_{PH} 11 Hz). $\delta(^{13}C)$ 32.88 (d, J_{PC} 135 Hz, CH), 52.37 (s, OMe), 52.88 (d, J_{PC} 7 Hz, (POMe), 165.49 (d, J_{PC} 5 Hz, C = O).

Dimethyl 1,2,2-Tris(methoxycarbonyl)ethylphosphonate (138; R,R',R" = Me).

To a slurry of 50% sodium hydride (1.18 g, 0.025 mol) in 1,2-dimethoxyethane (25 cm^3) at 20 °C was added with stirring trimethylphosphonoacetate (4.5 g, 0.025 mol). The solution was then stirred until the evolution of gas ceased. Bromine (3.95 g, 0.25 mol) was then added dropwise at such a rate that the temperature of the mixture did not rise above 20 °C. A white suspension resulted.

A suspension of the sodium salt of dimethylmalonate [prepared from dimethylmalonate (3.26 g, 0.025 mol) and 50% sodium hydride (1.18 g, 0.025 mol) in 1,2-dimethoxyethane (25 cm^3) at 20 °C] was then added dropwise over 1.5 h at 20 °C. The solution was then filtered and the solvent removed under reduced pressure (16 mm Hg, 50 °C bath) to leave an oil. Preparative layer chromatography on silica gel using ethyl acetate as eluant enabled the phosphonate to be isolated as a white solid (0.75 g, 9.6%), m.p. 76-77 °C. [Found: C, 38.5; H, 5.35. $C_{10}H_{17}O_9P$ requires C, 38.5; H, 5.5%]. The phosphonate was spectroscopically identical to the phosphonate (138; R,R',R" = Me) when prepared via the phosphorane (136; R,R' = Me). For ^{13}C n.m.r. spectral data for the phosphonate (138; R,R',R" = Me) see Table 32.

Thermal rearrangement of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrialkoxyphosphoranes (136).

Dimethyl 2,5-Dimethoxy-3-methoxycarbonyl-4-furanylphosphonate (146; R = Me).

A solution of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me) (13.73 g, 4.7 x 10^{-2} mol) in toluene (25 cm^3) was heated under reflux over 24 h. ^{31}P N.m.r. spectroscopy confirmed that none of the starting phosphorane remained in the mixture. The solvent was removed under reduced pressure (16 mm Hg, 50 °C) and volatile components removed by exhaustive pumping under reduced pressure (0.01 mm Hg, 50 °C bath) over 2 h. ^{31}P N.m.r. spectroscopy of the resulting oil (11.52 g) showed an essentially quantitative preparation of the desired furan at δ_P 13.58. Attempts to purfity the oil by medium pressure liquid chromatography on silica gel using a mixture of petroleum ether (60-80 °C) and ethyl acetate, 2:1 ratio, resulted in considerable retention and decomposition of the material on the column. Two components were isolated: a white crystalline solid, tetramethyl 3,6-dimethoxybenzene-1,2,4,5-tetracarboxylate (145) (0.6 g, 3.5%) and dimethyl 2,5-dimethoxy-3-methoxycarbonyl-4-furanylphosphonate (146; R = Me) (3.54 g, 26%).

Tetramethyl 3,6-dimethoxybenzene-1,2,4,5-tetracarboxylate (145), m.p. 119-121 °C. [Found: C, 51.9; H, 4.9. $C_{16}H_{18}O_{10}$ requires C, 51.6; H, 4.9%). M/e (relative intensity): M^+, 370 (88%), 340 (93%), 309 (100%), 324 (9%), 295 (24%). U.v. (methanol) 6.8 x 10^{-3} mg cm^3 λ_{max} n.m. (ϵ mol^{-1} dm^2): 208 (272309), 306 (38123). I.r. (chloroform) cm^{-1}: 3040, 2950, 1748, 1165. $\delta(^1H)$ 3.85 (s, 1H) 3.90 (br. s, 2H). $\delta(^{13}C)$ 52.94 (q, J_{CH} 148 Hz, CO_2Me), 64.29 (q, J_{CH} 146 Hz, OMe), 130.17 (C-1), 151.46 (q, J_{CH}, 4 Hz, C-3), 164.45 (q, J_{CH}, 4 Hz, C = O).

Dimethyl 2,5-dimethoxy-3-methoxycarbonyl-4-furanylphosphonate (146; R = Me). B.p. 102-120 °C 0.03 mm Hg. [Found: C, 40-9; H, 5.2. $C_{10}H_{15}O_8P$ requires C, 40.8; H, 5.15%]. $\delta(^{31}P)$ 13.6 (multiplicity from proton-coupled spectrum septet). $\delta(^1H)$ 3.56, (s, 6H), 3.76, (s, 3H), 3.84 (s, 3H), 3.99 (s, 3H). $\delta(^{13}C)$ 51.48, 52.81 (d, J_{PC} 6 Hz), 59.74, 60.28, 85.20 (d, J_{PC} 223 Hz , C-2), 93.30 (d, J_{PC} 10 Hz, C-3), 155.54 (d, J_{PC} 15 Hz, C-4), 155.06 (d, J_{PC} 17 Hz, C-5).

Diethyl 2,5-Dimethoxy-3-ethoxycarbonyl-4-furanylphosphonate (146; R = Et).

The furan (146; R = Et) was prepared from 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetriethoxyphosphorane (136; R = Et, R' = Me) by a similar procedure to that used for the preparation of the furan (146; R = Me) using the phosphorane (136; R= Me). The furan was isolated in almost quantitative yield as an oil $\delta(^{31}P)$ 13.4.

Formation of novel furans from reaction of aldehydes with 5-alkoxy-4-alkoxycarbonyl-2,3-dihydro-3-furanylidenephosphoranes.

Dimethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Me).

A solution of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me) (2,94 g, 0.01 mol) in toluene (25 cm^3) was heated under reflux with 4-nitrobenzaldehyde (0.82 g, 5 x 10^{-3} mol) for 30 mins. On cooling the precipitate formed was filtered off and washed with toluene. Recrystallisation from toluene gave the furan (131; R,R' = Me) (1.13 g, 67.3%), m.p. 179-181 °C. [Found: C, 53.5; H, 3.8; N, 4.1. $C_{15}H_{13}O_8N$ requires C, 53.7; H, 3.9; N, 4.2%]. $\delta(^1H)$ 3.76 (s, 3H), 3.91 (s, 3H), 4.21 (s, 3H), 7.70 (d, 9 Hz), 8.19 (d, 9 Hz). For ^{13}C n.m.r. spectral data see Table 26.

Diethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R = Me, R' = Et).

This material was prepared from 5-ethoxy-4-ethoxycarbonyl-2,3-dihydro-3-furanylidenetrimethoxyphosphorane (136; R = Me, R' = Et) by the method used to prepare the furan (131; R,R' = Me). Yield 2.29 g, 78.8%, m.p. 170-172 °C (sublimes). [Found: C, 56.1; H, 4.8; N, 3.9. $C_{17}H_{17}O_8N$ requires C, 56.2; H, 4.7; N, 3.85%]. $\delta(^1H)$ 1.30 (t, 7 Hz), 1.36 (t, 7 Hz), 4.21 (s), 4.26 (q, 7 Hz), 4.37 (q, 6 Hz), 7.68 (d, 9 Hz), 8.14 (d, 9 Hz). For ^{13}C n.m.r. spectral data see Table 28.

Dimethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R = Et, R' = Me).

This material was prepared from 2,3-dihydro-5-methoxy-4--methoxycarbonyl-3-furanylidenetriethoxyphosphorane (136; R = Et, R' = Me) by the method used to prepare the furan (131; R,R' = Me). On this occasion the reaction mixture was heated under reflux for 1 h. Recrystallisation from toluene gave the furan (131; R = Et, R' = Me) (1.25 g, 54.1%), m.p. 147-148 °C. [Found: C, 55.1; H, 4.2; N, 3.7. $C_{16}H_{15}O_8N$ requires C, 55.0; H, 4.3; N, 4.0%]. $\delta(^1H)$ 1.51 (t, 7 Hz), 3.76 (s), 3.90 (s), 4.53, (q, 7 Hz), 7.12 (d, 9 Hz), 8.1 (d, 9 Hz). For ^{13}C n.m.r. spectral data see Table 28.

Diethyl 5-Ethoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Et).

This furan (131; R,R' = Et) was prepared from 5-ethoxy--4-ethoxycarbonyl-2,3-dihydro-3-furanylidenetriethoxyphosphorane (136; R,R' = Et) by the method used to prepare the furan (131; R,R' = Me). Yield 1.16 g, 46.4%, m.p. 119-119.5 °C. [Found: C, 57.0; H, 4.95; N, 3.7. $C_{18}H_{19}O_2N$ requires C, 57.3; H, 5.1; N, 3.7%]. $\delta(^1H)$ 1.30 (t, 7 Hz), 1.35 (t, 7 Hz), 1.51 (t, 7 Hz), 4.04-4.70 (m), 7.65 (d, 9 Hz), 8.1 (d, 9 Hz). For ^{13}C n.m.r. spectral data see Table 28.

Dimethyl 2-(4-nitrophenyl)-5-isopropoxyfuran-3,4-dicarboxylate (131; R = Pr^i, R' = Me).

This furan (131; R = Pr^i, R' = Me) was prepared from 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetriisopropoxyphosphorane (136; R = Pr^i, R' = Me) by the method used to prepare the furan (131; R,R' = Me). The reaction mixture in this case was heated under reflux for 5 h. Yield 0.51 g, 40.1%, m.p. 137.5-140 °C. [Found: C, 56.4; H, 4.9; N, 3.7. $C_{17}H_{17}NO_8$ requires C, 56.2; H, 4.7; N, 3.85%]. $\delta(^1H)$ 1.47 (d, 6 Hz), 3.81 (d, 8 Hz), 5.02 (septet, 6 Hz), 7.63 (d, 9 Hz), 8.10 (d, 9 Hz). For ^{13}C n.m.r. spectral data see Table 28.

Dimethyl 2-(4-bromophenyl)-5-methoxyfuran-3,4-dicarboxylate.

A solution of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3--furanylidenetrimethoxyphosphorane (136; R,R' = Me) (0.01 mol) in toluene (25 cm^3) was heated under reflux for 1 h with 4-bromobenzaldehyde (0.95 g, 5 x 10^{-3} mol). The solvent was then removed under reduced pressure (16 mm Hg, 50 °C bath) and the resultant oil chromatographed (alumina, grade IV) using ethyl acetate : petroleum ether (60-80 °C) 1:1 as eluant to give the desired furan (1.01 g, 54.6%), m.p. 109-110 °C. [Found: C, 48.6; H, 3.5. $C_{15}H_{13}O_6Br$ requires C, 48.8; H, 3.5%). $\delta(^1H)$ 3.80, 3.88, 4.17, 7.47. For ^{13}C n.m.r. spectral data see Table 29.

Dimethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Me).

To a solution of 2,3-dihydro-5-methoxy-4-methoxycarbonyl--3-furanylidene(dimethoxyphenyl)phosphorane (0.25 g, 7.3 x 10^{-4} mol) in toluene (1 cm^3) was added 4-nitrobenzaldehyde (0.06 g, 4 x 10^{-4} mol) and the mixture allowed to stand overnight. The precipitate which formed was filtered off and recrystallised from toluene. The product, the furan (131; R,R' = Me) (0.02 g, 17%) was shown by n.m.r. spectroscopy and mixed melting point to be the same as that prepared from the phosphorane (136; R,R' = Me). M.p. 179-181 °C. [Found: C, 53.5; H, 3.7; N, 4.2. $C_{15}H_{13}O_8N$ requires C, 53.7; H, 3.9; N, 4.2%].

Synthesis of dimethyl and diethyl 5-methoxy-2-(4-nitrophenyl) furan-3,4-dicarboxylate (131; R = Me, R' = Me, Et).

N-(4-nitrobenzoyl)glycine.

To a cooled solution of glycine (24 g, 0.32 mol) in 5% aqueous sodium hydroxide (800 cm^3) was added sodium bicarbonate (53.8 g, 0.64 mol) followed by finely powdered 4-nitrobenzoylchloride (65.4 g, 0.35 mol; freshly sublimed) with vigorous stirring. Stirring was continued for a further 1 h during which time the temperature of the mixture was kept below 20 °C by cooling in an ice-water bath. Undissolved material was then filtered off and to the resulting solution was cautiously added an excess of 20% hydrochloric acid (590 cm^3). This caused the clear brick-red colouration of the solution to be discharged and a pink solid precipitated. The precipitate was allowed to settle over 2 h then filtered off, recrystallised from water and dried in a desiccator. Yield 45.8 g, 63.8%, m.p. 119-121 °C. [Found: C, 48.2; H, 3.3; N, 12.7. $C_9H_8O_5N_2$ requires C, 48.2; H, 3.6; N, 12.5%]. $\delta(^1H)$ ([$^2H_6$] dimethyl sulphoxide, external TMS) 3.86 (d, 6 Hz), 8.00 (d, 9 Hz), 8.20 (d, 9 Hz), 9.10 (t, 6 Hz replaceable proton).

Methyl N-(4-nitrobenzoyl)glycine (134).

A solution of N-(4-nitrobenzoyl)glycine (20 g, 0.01 mol) in methanol (120 cm^3) together with concentrated sulphuric acid (3 cm^3) was placed under reflux for 2 h. After cooling to room temperature crystallisation occurred. The solid was filtered off, washed with water, then recrystallised from methanol to give the desired product (20.34 g, 95.7%), m.p. 152-153 °C. [Found: C, 50.55; H, 4.1; N, 11.8. $C_{10}H_{10}O_5N_2$ requires C, 50.4; H, 4.2; N, 11.75%]. $\delta(^1H)$ ([^{2}H]chloroform) 3.79 (s), 4.22 (d, 5 Hz), 6.77 (br s), 7.94 (d, 9 Hz), 8.23 (d, 9 Hz). $\delta(^{13}C)$ ([$^2H_6$]dimethyl sulphoxide) 41.32 (CH_2), 51.80 (-OCH_3), 123.44, 128.57, 138.90, 148.95 (Ar), 164.75, 169.71 (C = O).

5-Methoxy-2-(4-nitrophenyl)oxazole (133).

Methyl N-(4-nitrobenzoyl)glycine (134) (2.5 g, 0.01 mol) and phosphorus pentoxide (2.1 g, 0.01 mol) were dissolved in chloroform (25 cm^3; alcohol free) then heated under reflux.

The progress of the reaction was monitored by proton n.m.r. spectroscopy. After 71 hrs the resulting solution was neutralised with 20% potassium hydroxide solution and extracted with benzene (4 x 50 cm^3). The benzene extract was dried ($MgSO_4$) and the solvent removed under reduced pressure (16 mm Hg, 50 °C) to give an orange solid. Recrystallisation from toluene gave the pure oxazole (1.7 g, 74%) m.p. 84 °C.[Found: C, 54.65; H, 3.7; N, 12.85%; M^+, 220. $C_{10}H_8O_4N_2$ requires C, 54.55; H, 3.7; N, 12.7; M, 220]. $\delta(^1H)$ 3.96 (s), 6.27 (s), 7.95 (d, 9 Hz), 8.18 (d, 9 Hz). $\delta(^{13}C)$ 58.82 (q, 147 Hz, OCH_3), 100.96 (d, 198 Hz, C-4), 150.12 (complex, C-2), 161.48 (d of d, complex, C-5), 124.01 (d of d, 4 Hz, 170 Hz), 125.62 (d of d, 6 Hz, 168 Hz), 132.67 (t, 8 Hz), 147 (complex, Ar).

Dimethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Me).

A suspension of 5-methoxy-2-(4-nitrophenyl)oxazole (133) (0.2 g, 9.1×10^{-4} mol) in dimethyl acetylenedicarboxylate (1.5 g, 0.01 mol) was heated at 120 °C in an oil bath for 12 h. The mixture was then allowed to cool and a precipitate formed on standing. The excess dimethyl acetylenedicarboxylate was removed under reduced pressure (0.01 mm Hg, room temperature) and the resulting solid recrystallised from toluene. The product (0.04 g, 13%) had the same spectral analysis, melting point and mixed melting point as the dimethyl 5-methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Me) produced from the reaction of 2,3-dihydro-5-methoxy--4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me) and 4-nitrobenzaldehyde (see Experimental p.280). M.p. 179-181 °C. [Found: C, 53.5; H, 3.8; N, 3.95. $C_{15}H_{13}O_8N$ requires C, 53.7; H, 3.9; N, 4.2%]. For ^{13}C n.m.r. spectral data see Table 26.

Diethyl 5-Methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R = Me, R' = Et).

A suspension of 5-methoxy-2-(4-nitrophenyl)oxazole (133) (0.2 g, 9.1×10^{-4} mol) in diethyl acetylenedicarboxylate (2 g, 0.01 mol) was heated at 110 °C for 30 h, whilst monitoring the progress of the reaction by proton n.m.r. spectroscopy. The solvent was then reduced under reduced pressure (0.01 mm Hg, room temperature) and toluene (3 cm^3) added to the resulting oil. The precipitate which formed was filtered off and recrystallised from toluene. The product (0.03 g, 9%) had the same spectral characteristics as the furan (131; R = Me, R' = Et) produced from the reaction of

5-ethoxy-4-ethoxycarbonyl-2,3-dihydro-3-furanylidenetrimethoxyphosphorane (136; R = Me, R' = Et). M.p. 170-172 °C. [Found: C, 56.2; H, 4.8; N, 3.43. $C_{17}H_{17}O_8N$ requires C, 56.2; H, 4.7; N, 3.85%]. For ^{13}C n.m.r. spectral data see Table 28.

Attempted reactions of 2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me) with aromatic ketones.

1.1 With 2,2,2-trifluoroacetophenone.

A solution of the phosphorane (136; R,R' = Me) (0.6 g, 2 x 10^{-3} mol) and trifluoroacetophenone(0.35 g, 2 x 10^{-3} mol) in toluene (5 cm^3) was heated with stirring at 100 °C under reflux overnight. No reaction occurred with the ketone which was recovered. However, rearrangement of the phosphorane (136; R,R' = Me) to the furan (146; R = Me) had occurred and this was confirmed by ^{31}P n.m.r. spectroscopy.

1.2 With acetophenone.

An equimolar solution of the phosphorane (136; R,R' = Me) (0.2 g, 7.4 x 10^{-4} mol) and acetophenone (0.09 g) in toluene (5 cm^3) was heated with stirring at 100 °C under nitrogen overnight. ^{31}P N.m.r. spectroscopy indicated that thermal rearrangement of the phosphorane (136; R,R' = Me) had occurred. The acetophenone was recovered from the mixture.

1.3 With 4-nitroacetophenone.

A solution of the phosphorane (136; R,R' = Me) (2.94 g, 0.01 mol) and 4-nitroacetophenone (1.65 g, 0.01 mol) was heated under reflux in toluene (20 cm^3) overnight. No reaction with the ketone occurred although ^{31}P n.mr. spectroscopy confirmed that rearrangement of the phosphorane (136; R,R' = Me) had occurred.

Attempted reaction of 1-ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R' = Me, R" = Et) with 4-nitrobenzaldehyde.

A solution of the phosphorane (142; R,R' = Me, R" = Et) (0.5 g, 1.2×10^{-3} mol) and 4-nitrobenzaldehyde (0.18 g, 1.2×10^{-3} mol) in toluene (5 cm^3) was heated under reflux for 21 h. ^{31}P N.m.r. spectroscopy indicated that no reaction had occurred with the aldehyde which was recovered from the mixture.

Attempted cyclisation of dimethyl 1,2,2-tris(methoxycarbonyl)-ethylphosphonate (138; R,R',R" = Me) to give the furan, dimethyl 2,5-dimethyl-3-methoxycarbonyl-4-furanyl-phosphonate (146; R = Me).

1.1 With phosphorus pentachloride.

A solution of the phosphonate (138; R,R',R" = Me) (0.5 g, 1.6×10^{-3} mol) in chloroform (20 cm^3, alcohol free) was treated with phosphorus pentachloride (0.33 g, 1.6×10^{-3} mol) and placed under reflux for 24 h. The mixture was then cooled in an ice-bath and potassium hydroxide (20%, 25 cm^3) added with stirring. The mixture was then extracted with chloroform (3 x 25 cm^3). The pooled chloroform extract was dried ($MgSO_4$) and the solvent removed under reduced pressure (50 °C bath, 15 mm Hg) leaving an oil. ^{31}P N.m.r. spectroscopy showed that decomposition of the phosphonate (138; R,R',R" = Me) had occurred but, there was no evidence for the formation of the desired furan (146; R,R' = Me).

1.2 With phosphorus pentoxide.

The cyclisation of the phosphonate (138; R,R',R" = Me) was also attempted using phosphorus pentoxide by the same method as that previously described for phosphorus pentachloride. Once again decomposition of the phosphonate (138; R,R',R" = Me) occurred but, there was no sign of the formation of the desired furan (146; R,R' = Me).

Attempted synthesis of diethyl 3-ethoxycarbonyl-2,5-dimethoxy-4-furanylphosphonate (148).

2,3-Dibromopropenoate.

A solution of ethyl propiolate (5 g, 0.05 mol) in carbon tetrachloride (20 cm^3) at 65 °C was treated with a solution of bromine (8.16 g, 0.05 mol) in carbon tetrachloride (5 cm^3) over 1½ h. The mixture was stirred for a further ½ h and then the solvent was removed under reduced pressure (16 mm Hg, 50 °C) to give a quantitative yield of 2,3-dibromopropenoate (13.13 g, 100%) as a mixture of E and Z isomers, 3:7 ratio. [Found: C, 23.1; H, 2.4. $C_5H_6Br_2O_2$ requires C, 23.3; H, 2.35%]. $\delta(^1H)$ Z isomer: 1.31 (t, 7 Hz), 4.27 (q, 7 Hz), 8.14 (s). E isomer: 1.34 (t, 7 Hz), 4.29 (q, 7 Hz), 7.06 (s).

Ethyl (3-diethoxyphosphinyl)-2-bromopropenoate.

A solution of 2,3-dibromopropenoate (11 g, 0.04 mol) in triethyl phosphite (14.8 g, 0.08 mol) was stirred and heated in an oil bath at 100 °C for 3 h. As ethyl bromide formed it was allowed to distil from the reaction flask. Volatile components were then removed under reduced pressure (16 mm Hg, 50 °C) and the resulting liquid distilled to give the product (9.7 g, 72%), b.p. 98-100 °C, 0.03 mm Hg as a mixture of Z:E isomers in 4:1 ratio. [Found: C, 34.4; H, 5.3. $C_9H_{16}BrO_5P$ requires C, 34.3; H, 5.1%]. Z isomer: $\delta(^{31}P)$ 10.52 (heptet, J_{PH} 9 Hz). $\delta(^1H)$ 1.34 (t, 7 Hz), 1.37

(t, 7 Hz), 4.10 (q, 7 Hz), 4.26 (d of q, J_{PH} 3 Hz, J_{HH} 7 Hz), 7.46 (d, J_{PH} 10 Hz). $\delta(^{13}C)$ 14.01 (CH_3), 16.35 (d, J_{PC} 7 Hz, $POCH_2CH_3$), 62.73 (d, J_{PC} 5 Hz, $POCH_2$), 63.55 (OCH_2), 130.85 (d, J_{PC} 192 Hz, α-C), 129.41 (β-C), 160.9 (d, J_{PC} 22 Hz, C = O). E isomer: $\delta(^{31}P)$ 9.47 (heptet, J_{PH} 9 Hz). $\delta(^{1}H)$ 1.35 (t, 7 Hz), 1.35 (t, 7 Hz), 4.03 (q, 7 Hz), 4.22 (d of q, J_{PH} 9 Hz, J_{HH} 7 Hz), 6.37 (d, J_{PH} 8 Hz). $\delta(^{13}C)$ 13.77 (CH_3), 16.27 (d, J_{PC} 6 Hz, $POCH_2CH_3$), 62.59 (d, J_{PC} 5 Hz, $POCH_2$), 62.91 (OCH_2), 125.39 (d, J_{PC} 178 Hz, α-C), 126.27 (β-C), 162.83 (d, J_{PC} 7 Hz, C = O).

Ethyl (diethoxyphosphinyl)propynoate (147).

A solution of ethyl (3-diethoxyphosphinyl)-2-bromopropenoate (9.45 g, 3 x 10^{-2} mol) in dry diethyl ether (30 cm^3) was heated under reflux overnight with triethylamine (5 g, 0.05 mol). The precipitated hydrobromide was filtered off and the solvent removed from the resulting solution under diminished pressure (16 mm Hg, 40 °C). The resulting oil was then distilled to give the propynoate (4.51 g, (65%), b.p. 103 °C 0.01 mm Hg (Lit.,[76] b.p. 128-130 °C 0.1 mm Hg). [Found: C, 45.95; H, 6.7. $C_9H_{15}O_5P$ requires C, 46.1; H, 6.5%]. $\delta(^{31}P)$ -9.6 (quintet, 9 Hz). $\delta(^{1}H)$ 1.37 (d of t, J_{PH} 4 Hz, J_{HH} 7 Hz), 4.13 (q, 7 Hz), 4.29 (q, 7 Hz).

2,5-Dibromofuran.[79]

To an aqueous solution of sodium 5-bromofuran-2-carboxylate [prepared from 5-bromo-2-furancarboxylic acid (10 g, 2 x 10^{-2} mol) and sodium hydroxide (5.44 g) in water (44 cm^3)] was added dropwise with stirring a solution of bromine (8.4 g, 5.2 x 10^{-2} mol) in aqueous potassium bromide (2M, 25 cm^3). Stirring was continued until the effervescence had ceased. The mixture was then brought to the boil and after cooling allowed to stand overnight. The buff coloured precipitate which formed was extracted into diethyl ether (3 x 75 cm^3). The pooled ether extract was dried ($MgSO_4$) and the ether then removed at room temperature under reduced pressure (16 mm Hg) to leave 2,5-dibromofuran (6.4 g, 55%). $\delta(^1H)$ ([^2H]chloroform) 6.28, ([$^2H_6$]dimethyl sulphoxide) 6.60, (Lit., (CCl_4) 6.25,[80] ([^2H]chloroform) 6.37.[81]

2,5-Dimethoxyfuran.

To a stirred solution of 2,5-dibromofuran (6.4 g, 0.03 mol) in methanol (10 cm^3) was added sodium methoxide (0.06 mol). The mixture was then allowed to stand overnight. The precipitate which had formed was filtered off and the solvent removed from the resulting yellow filtrate under reduced pressure (16 mm Hg, room temperature). This resulted in the formation of an unstable material which was identified as 2,5-dimethoxyfuran. $\delta(^1H)$ ([$^2H_4$]methanol) 3.32 (s, OMe), 5.35 (s, CH).

Preparations involving the use of carbon-13 enriched carbon dioxide.

5[^{13}C]-2,2-Dimethoxy-3,4-bismethoxycarbonyl-5-oxo-2-phenyl-Δ^3-oxaphospholene (122; R = Ph, R' = OMe, 5[^{13}C]).

To an agitated solution of dimethyl acetylenedicarboxylate (0.22 g, 1.56 x 10^{-3} mol) in [^2H]chloroform (1 cm^3) in a specially constructed vessel [see Fig. 30], previously charged with carbon-13 enriched carbon dioxide gas (90%, 40 cm^3, 1.78 x 10^{-3} mol), was slowly added, using a syringe, a solution of dimethyl phenylphosphonite (0.25g, 1.56 x 10^{-3} mol) in [^2H]chloroform (1.5 cm^3). The ^{31}P n.m.r. spectrum of the resulting solution showed the presence of the oxaphospholene (122; R = Ph, R' = OMe, 5[^{13}C]) in an almost quantitative yield. $\delta(^{31}P)$ -37.0 (d, J_{PC} 10 Hz). $\delta(^{13}C)$ 158.47 (d, J_{CP} 10 Hz). $\delta(^{13}C)$ {^{31}P -37.0} 158.47 (s). $\delta(^{13}C)$ {^{31}P -38.0} 158.47 (br. s).

5[^{13}C]-2,2,2-Trimethoxy-3,4-bismethoxycarbonyl-5-oxo-Δ^3-oxaphospholene (108; R = Me, 5[^{13}C]).

The oxaphospholene (108; R = Me, 5[^{13}C] was prepared by the method previously described for the oxaphospholene (122; R = Ph, R' = OMe, 5[^{13}C]) using trimethyl phosphite (0.19 g, 1.5 x 10^{-3} mol). ^{31}P N.m.r. spectroscopy showed the oxaphospholene (108; R = Me, 5[^{13}C]) at δ_P -50.9 (d, J_{PC} 10 Hz).

Isotopically labelled 5[^{13}C]-4[^{13}C=O]-2,3,-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me, 5[^{13}C], 4[^{13}C=O]).

To a solution of dimethyl acetylenedicarboxylate (0.22 g, 1.5 x 10^{-3} mol) in [^2H]chloroform (0.5 cm^3) in a specially constructed vessel [see Fig. 30] and charged with carbon-13 enriched carbon dioxide (90%, 40 cm^3, 1.78 x 10^{-3} mol) was added, with vigorous shaking, a solution of trimethyl phosphite (0.38 g, 3.0 x 10^{-3} mol) in [^2H]chloroform (1.5 cm^3). ^{31}P N.m.r. spectroscopy showed the product to be the required phosphorane (136; R,R' = Me , 5[^{13}C], 4[^{13}C=O]) in an almost quantitative yield. $\delta(^{31}P)$ 47.4 (d, J_{PC} 21 Hz). $\delta(^{13}C)$ 163.45 (s), 154.52 (d, J_{CP} 21 Hz), 86.09 (d, J_{CC} 90 Hz), see Table 31.

Isotopically labelled 5[^{13}C]-4[^{13}C=O]-2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenedimethoxyphenylphosphorane.

This phosphorane was prepared by the method previously described for the preparation of the phosphorane (136; R,R' = Me, 5[^{13}C], 4[^{13}C=O]) using dimethyl phenylphosphonite (0.5 g, 3.0 x 10^{-3} mol) in place of trimethyl phosphite. $\delta(^{31}P)$ 65.3 (d, J_{PC} 19 Hz). $\delta(^{13}C)$ 162.48 (s), 154.03 (d, J_{CP} 19 Hz).

Isotopically labelled dimethyl 5[^{13}C]-4[^{13}C=O]-5-methoxy-2-(4-nitrophenyl)furan-3,4-dicarboxylate (131; R,R' = Me, 5[^{13}C], 4[^{13}C=O]).

A solution of isotopically labelled 5[^{13}C]-4[^{13}C=O]-2,3-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me, 5[^{13}C], 4[^{13}C=O]) (1.4×10^{-3} mol) and 4-nitrobenzaldehyde (0.12 g, 7×10^{-4} mol) in toluene (2.5 cm^3) was heated under reflux for 1½ h. On cooling a solid precipitated from solution, this was filtered off, washed with toluene and finally recrystallised from toluene to give the furan (131; R,R' = Me, 5[^{13}C], 4[^{13}C=O]) (0.06 g, 26%), m.p. 180 °C. [Found: C, 53.9; H, 3.8; N, 4.2. $C_{13}{}^{13}C_2H_{13}NO_8$ requires C, 54.0; H, 3.9; N, 4.15%]. The structure of the furan (131; R,R' = Me, 5[^{13}C], 4[^{13}C=O]) was confirmed by ^{13}C n.m.r. spectroscopy by comparison with a sample of unlabelled material (131; R,R' = Me). $\delta(^{13}C)$ 161.53 (s, 4[^{13}C=O], 161.27 (s, 5[^{13}C]), 93.14 (d, J_{CC} 90 Hz, C-4), see Table 26.

Isotopically labelled 2[^{13}C=O]-1-ethoxycarbonyl-2,2-bis-(methoxycarbonyl)ethylidenetrimethoxyphosphorane (142; R,R' = Me, R" = Et, 2[^{13}C=O]).

To a solution of isotopically labelled 5[^{13}C]-4[^{13}C=O]-2,3,-dihydro-5-methoxy-4-methoxycarbonyl-3-furanylidenetrimethoxyphosphorane (136; R,R' = Me, 5[^{13}C], 4[^{13}C=O]) (0.52 g, 1.56×10^{-3} mol) in toluene (1.5 cm^3) was added ethanol (0.08 g) and the flask then shaken. ^{31}P N.m.r. spectroscopy showed the formation of the phosphorane (142; R,R' = Me, R" = Et, 2[^{13}C=O]), as two broad signals. Major rotamer: δ_P ([$^2H_8$]toluene) 59.0 (s).

$\delta(^{13}C)$ 172.08 (2[^{13}C=O]), 171.43 (2[^{13}C=O]). Minor rotamer: δ_P ([$^2H_8$]toluene) 56.66 (s). $\delta(^{13}C)$ 171.72 (2[^{13}C=O]), 171.02 (2[^{13}C=O]), see Table 36.

Isotopically labelled 2[^{13}C=O]-1-ethoxycarbonyl-2,2-bis(methoxycarbonyl)ethylidenetriethoxyphosphorane (142; R,R" = Et, R' = Me, 2[^{13}C=O]).

The isotopically labelled phosphorane (142; R,R" = Et, R' = Me, 2[^{13}C=O]) was prepared in an almost quantitative yield by reacting the isotopically labelled phosphorane (136; R = Et, R' = Me, 5[^{13}C], 4[^{13}C=O]) with ethanol. $\delta(^{31}P)$ ([$^2H_8$]toluene) 53.7 (major rotamer), 51.9 (minor rotamer). For ^{13}C n.m.r. spectral data see Table 36.

Isotopically labelled 2[^{13}C=O]-1,2,2-tris(methoxycarbonyl)-ethylidenetriethoxyphosphorane (142; R = Et, R',R" = Me, 2[^{13}C=O]).

The phosphorane (142; R = Et, R',R" = Me, 2[^{13}C=O]) was prepared by the method previously described for the phosphorane (142; R,R' = Me, R" = Et, 2[^{13}C=O]) by reacting the isotopically labelled phosphorane (136; R = Et, R' = Me, 5[^{13}C], 4[^{13}C=O]) with methanol. $\delta(^{31}P)$ ([$^2H_8$]toluene) 53.1 (major rotamer), 51.1 (minor rotamer).

PREPARATIONS INVOLVING THE USE OF ELEMENTAL SULPHUR.

Dimethyl 1,2-Bis(methoxycarbonyl)-2-(methylthio)ethylidenephosphonate (104; R = Me).

A solution of trimethyl phosphite (0.13 g, 1 mmol) in dry benzene (0.5 cm^3) was rapidly mixed with a solution of dimethyl acetylenedicarboxylate (0.14 g, 1 mmol) in benzene (1 cm^3) to which flowers of sulphur (0.03 g, 1 mmol) had been added. The products from three such reactions were then pooled and filtered to remove the excess sulphur. The ^{31}P n.m.r. spectrum of the resulting solution showed the presence of both the thioketone, 1,2-bis(methoxycarbonyl)-2-(thioxo)ethylidenetrimethoxyphosphorane (103; R = Me) (δ_P 45.3, decet, 7 Hz), and its rearrangement product, dimethyl 1,2-bis(methoxycarbonyl)-2-(methylthio)ethylidenephosphonate (104) in addition to trimethyl thiophosphate. After about 4 h at room temperature the rearrangement was complete. The solvent was removed under reduced pressure (40 °C at 16 mm Hg) and the resulting oil was chromatographed on silica gel using a 3:2 chloroform:ethyl acetate mixture as the eluant. The desired phosphonate (104) (6.28 g, 31%) was obtained as an oil, $\delta(^{31}P)$ 15.1 (J_{PH} septet). [Found: C, 36.4; H, 5.0. $C_9H_{15}O_7PS$ requires C, 36.2; H, 5.0%]. $\delta(^1H)$ 2.29 (3H, SMe), 3.70 (d, 5 Hz, 6H, POMe), 3.85 (6H, OMe). For ^{13}C n.m.r. spectral data see Table 15.

1,2-Bis(methoxycarbonyl)-2-(thioxo)ethylidenetriethoxyphosphorane (103; R = Et).

A solution of triethyl phosphite (0.35 g, 2.1 x 10^{-3} mol) in dry benzene (0.5 cm^3) was rapidly added with shaking to the bottom of a solution of dimethyl acetylenedicarboxylate (0.14 g, 1 x 10^{-3} mol) in benzene (1 cm^3) to which flowers of sulphur (0.1 g) had been added.

^{31}P N.m.r. spectroscopy showed the presence of two products, triethyl thiophosphate (δ_P 71.9) and the phosphorane (103; R = Et) δ_P([$^2H_6$]benzene) 37.5 (sept, $^3J_{PH}$ 7 Hz). For ^{13}C n.m.r. spectral data see Table 14. Attempts to obtain a pure sample of the phosphorane (103; R = Et) at this time were unsuccessful. More recently,[64] attempts to purify the phosphorane (103; R = Et) by chromatography have been shown to lead to rearrangement to give the phosphonate, dimethyl 1,2-bis(methoxycarbonyl)-2-(methylthio)ethylidenephosphonate (106).

Diethyl 2-(Ethylthio)-1,2-bis(methoxycarbonyl)ethylidenephosphonate (106).

A solution of 1,2-bis(methoxycarbonyl)-2-(thioxo)ethylidenetriethoxyphosphorane (103; R = Et) (0.7 g, 2.1×10^{-3} mol) in benzene (10 cm^3) was heated under reflux and monitored by ^{31}P n.m.r. spectroscopy. ^{31}P N.m.r. spectroscopy showed that the phosphorane (103; R = Et) δ_P 37.5 p.p.m. rearranged (half life ∿5 h) to the desired phosphonate (106). When the rearrangement was complete the solvent was removed under reduced pressure (16 mm Hg, 50 °C bath) to give the phosphonate (106) as a mixture of *cis* and *trans* isomers $\delta(^{31}P)$ 11.71, 9.87 respectively, 7:3. For ^{13}C n.m.r. spectral data see Table 15. [Found: C, 42.6; H, 6.1%; M^+, 340. $C_{12}H_{21}O_7PS$ requires C, 42.35; H, 6.2%; M, 340].

PREPARATION OF ELECTROPHILIC ACETYLENES OTHER THAN DIMETHYL ACETYLENEDICARBOXYLATE.

Acetylenedicarboxamide.[82]

To a vigorously stirred solution of aqueous ammonia (50 cm^3; SG 0.88) cooled in an ice-bath was added dimethyl acetylenedicarboxylate (12 g, 0.08 mol). The mixture was then stirred for a further 2 h. The precipitated solid was filtered, washed with ethanol (10 cm^3) and dried in vacuo to give the diamide (8.74 g, 92.4%). [Found: C, 41.32; H, 4.36; N, 23.87. $C_4H_4N_2O_2$ requires C, 42.86; H, 3.60; N, 24.98%]. $\delta(^{13}C)$ ($[^2H_6]$dimethyl sulphoxide) 50.5, 152.8 (C=O).

Dicyanoacetylene (149).[82]

A mixture of acetylenedicarboxamide (6 g, 0.05 mol), phosphorus pentoxide (50 g) and fine white sand (50 g), was placed in a round--bottomed distillation flask (150 cm^3). The flask was placed under reduced pressure (0.06 mm Hg) and an oil bath at 215 °C was then quickly applied to the flask. A small quantity of the desired alkyne distilled from the flask and was collected in a receiver flask cooled in liquid nitrogen. $\delta(^{13}C)$ 55.02, 103.06 (CN).

Ethyl (diethoxyphosphinyl)propynoate (147).

For the preparation of ethyl (diethoxyphosphinyl)propynoate (147) see previous experimental p. 289.

Tetrahydro-2-(1-methylpropynoxy)-2H-pyran.

To a stirred mixture of but-1-yn-3-ol (34 g, 0.48 mol) and dihydropyran (41 g, 0.49 mol), cooled in an ice bath, was added phosphoryl chloride (0.15 g). The mixture was then stirred at room temperature overnight. Potassium hydroxide solution (10%, 10 cm^3) was then added and the mixture extracted with diethyl ether (3 x 100 cm^3). The ether extracts were pooled, dried (magnesium sulphate) and the ether then removed under reduced pressure (15 mm Hg, 50 °C) to leave the tetrahydropyranyl ether (58.7 g, 79%). δ(^{1}H) 1.46 (d, J 7 Hz), 2.37 (d, J 2 Hz), 4.53 (d of q, J 2 Hz, 7 Hz), 1.66 (br s), 3.25 - 4.15 (br m), 4.93 (br s).

Methyl 4-hydroxypent-2-ynoate.

A solution of the tetrahydropyranyl ether of but-1-yn-3-ol (58 g, 0.38 mol) in tetrahydrofuran (150 cm^3) was added dropwise to ethylmagnesium bromide [prepared from magnesium (10 g, 0.42 mol) and ethyl bromide (41.4 g, 0.38 mol)] in tetrahydrofuran (250 cm^3) under nitrogen. The mixture was stirred for a further 1 h then transferred to a pressure equalised dropping funnel under nitrogen. This mixtures was then added dropwise with stirring to methyl chloroformate (36 g, 0.38 mol) in tetrahydrofuran (150 cm^3) over 1 h. Dilute hydrochloric acid (1M, 20 cm^3) was then added and the resulting mixture extracted with diethyl ether (3 x 100 cm^3). The ether extracts were dried (magnesium sulphate) and the ether then removed under reduced pressure (15 mm Hg, 50 °C) leaving the tetrahydropyranyl ether of methyl 4-hydroxypent-2-ynoate (155). This was taken up in methanol (100 cm^3), and after the addition of hydrochloric acid (1M, 100 cm^3) the mixture was stirred for 12 h. The organic layer was removed and the aqueous layer extracted with diethyl ether (3 x 50 cm^3). The organic layer and ether extract were pooled, dried (magnesium sulphate) and the solvent then removed under reduced pressure (15 mm Hg, 50 °C) to leave an oil. This was distilled to give methyl 4-hydroxypent--2-ynoate (b.p. 75 °C, 0.1 mm Hg) (Lit.,[83] 60 °C 0.03 mm Hg, 114 °C, 12 mm Hg) (39.3 g, 80.7%). δ(^{1}H) 1.48 (3H, d, J 7 Hz, 4-Me), 3.11 (1H br s, OH) 3.73 (3H, s, OMe), 4.6 (1H, q, J 7 Hz, CH).

Methyl 4-oxo-pent-2-ynoate (155).

To a solution of methyl 4-hydroxypent-2-ynoate (10.8 g, 0.08 mol) in benzene (40 cm^3) was added dropwise over 1½ h chromic acid (80 cm^3, 3M). During this time the temperature of the mixture was maintained below 5 °C by cooling with an ice-water bath. The mixture was stirred for a further 1 h, then the benzene layer was decanted off, dried (magnesium sulphate) and the solvent removed under reduced pressure (15 mm Hg, 50 °C) to leave an oil. This oil was distilled over hydroquinone to give the acetylene (155) (b.p. 44 °C 3 mm Hg) (Lit.,[83] b.p. 79 °C, 16 mm) (2.21 g, 22%). $\delta(^1H)$ 2.4 (3H, s, Me), 3.80 (3H, s, OMe). [Found: C, 56.4; H, 4.78. $C_6H_6O_3$ requires C, 57.1; H, 4.8%].

Hex-3-yne-2,5-dione (156).

To a solution of hex-3-yne-2,5-diol (38 g, 0.33 mol) in benzene (450 cm^3) at about 5 °C, was added dropwise over 2 h chromic acid (100 cm^3) [prepared from sodium dichromate (65 g), concentrated sulphuric acid (95 cm^3) and water (400 cm^3)]. The mixture was allowed to stir for a further 1 h, then the organic layer was separated and the aqueous layer extracted with ether (3 x 50 cm^3). The combined organic solutions were dried (magnesium sulphate) and the solvent removed under reduced pressure to leave an oil. This oil (34 g), which contained hex-3-yne-2,5-diol (56%) and 5-hydroxyhex-3-yn-2-one (44%), was dissolved in benzene (400 cm^3) and hex-3-yne-2,5-diol (25 g) was then added. To this mixture was then added dropwise with stirring a further portion of chromic acid (100 cm^3). During this addition the reaction mixture was kept below 5 °C. Stirring was continued for 1 h and the resulting mixture worked up as previously described to give a mixture of hex-3-yne-2,5-diol (25%), 5-hydroxy

-hex-3-yn-2-one (67%), and hex-3-yne-2,5-dione (8%). Fractional distillation of this mixture gave the diketone (1.39 g, 2.3%), b.p. 40-52 °C, 0.22 mm Hg (Lit.,[84] 50 °C bath, 0.15 mm Hg); the hydroxyketone (17.28 g), b.p. 58-60 °C, 0.24 mm Hg (Lit.,[84] 50-75 °C, 0.2 mm Hg) and a mixture of the hydroxyketone (70%) and diketone (10%) (0.94 g). Hex-3-yne-2,5-dione $\delta(^1H)$ 1.41 (s). I.r. (chloroform) cm^{-1}: 2950, 2360, 1660. 5-Hydroxyhex-3-yne-2-one $\delta(^1H)$ 1.32 (3H, s, 1Me), 1.49 (3H, d, J 7 Hz, 5Me), 3.4 (1H, br s, OH), 4.62 (1H, q, J 7 Hz, CH).

Equipment

N.m.r. spectrometers

JEOL JNM-FX100 F.T.n.m.r. spectrometer

Hitachi Perkin-Elmer R24 and R24B n.m.r. spectrometers

Infrared spectrophotometer

Pye Unicam SP2000

U.V. spectrophotometer

Varian DMS 100

Cooling Unit

Neslab Instruments Inc., Cryocool CC-100

Autoclave

Berghof, 150 cm^3 polytetrafluoroethylene (PTFE) lined high pressure autoclave.

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